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Application of Artificial Intelligence In Identifying Antioxidants for Aging

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A B S T R A C T
Scientific research continuously illustrates that aging can be delayed, treated, or even avoided and, as a result, health can be maintained by consuming health-promoting antioxidants. Food, nutrition, nutrients, and the health advantages linked with them are becoming more important to consumers. As a result, a nutrition industry based on natural foods and antioxidants is emerging, with consumer decisions driving economic growth. Information technology, especially artificial intelligence (AI), is set to dramatically extend the field of skin aging therapies accessible to consumers by systematically finding and characterizing natural, effective, and safe bioactive compounds (bioactives) that address aging. A literature search was conducted using the keywords in PubMed: "deep learning antioxidant", "algorithms antioxidant", "neural networks antioxidant", "support vector machine antioxidant", "natural language processing antioxidant", "computer vision antioxidant", "artificial intelligence antioxidant", and "machine learning antioxidant". There were a total of 146 papers chosen for evaluation. This research only looked at full-text papers that were available for free. The relevance of the abstracts was determined, and 29 publications were judged to be relevant to the current study. To summarize, AI has the potential to help in a variety of antioxidant identification discovery fields. As with any concept, it is unlikely to be a panacea, but its use should be expanded to help scientists in their various roles and specialties throughout the process.

Keywords: *Artificial intelligence, ai, aging, antioxidants, anti-aging, bioactives, machine learning, deep learning.*

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INTRODUCTION
Scientific research continuously illustrates that aging can be delayed, treated, or even avoided and, as a result, health can be maintained by consuming health-promoting antioxidants. Food, nutrition, nutrients, and the health advantages linked with them are becoming more important to consumers.As a result, a nutrition industry based on natural foods and antioxidants is emerging, with consumer decisions driving economic growth. Information technology, especially artificial intelligence (AI), is set to dramatically extend the field of aging therapies accessible to consumers by systematically finding and characterizing natural, effective, and safe bioactive compounds (bioactives) that address aging [1].

For a variety of reasons, the beauty and skin care sectors have been slow to embrace AI technology for their substance development processes, resulting in a lack of viable methodologies for large-scale and increased molecular and biochemical component identification.The emergence of the AI-driven technological revolution enables thorough characterization and knowledge of the universe of antioxidant and therapeutic compounds, enabling unparalleled mining of the food and natural product space. As a consequence of this increase in bioactives, the consumer's antioxidant repertoire expands dramatically, ultimately leading to bioactives being produced particularly to meet unmet health requirements [1].

The application of artificial intelligence (AI) in the discovery of anti-aging antioxidants is the subject of this article. It provides a brief (re)introduction to the role of antioxidants in aging, the history of artificial intelligence in drug discovery, and the types of artificial Intelligence, machine learning and deep learning. It then attempts to review various studies published on the applications of AI techniques in antioxidant discovery.

BACKGROUND
A. Antioxidants and Aging
The biggest contact area between the human body and the external environment is the skin, which serves as a barrier between the human body and the environment. It offers an aesthetic impact in addition to protecting the body from external environmental harm and preventing water loss. Organ aging happens throughout our lives. The skin, being the biggest organ of the human body, exhibits apparent indications of aging as a result of age, UVR exposure, and chemical pollution. People are paying greater attention to skin aging and attempting to have a better knowledge of it as science and technology advance and human living standards rise. Cosmetics and pharmaceuticals for the treatment and prevention of

skin aging account up a major chunk of many people's daily spending, particularly women. This enormous demand continues to fuel research into skin aging prevention and therapy [2].

The two types of skin aging are chronological and photo-aging (or internal aging and external aging). The chronological aging of the skin happens throughout the body, whereas photo-aging occurs on the body's light-exposed regions, as the term implies. Internal causes cause chronological aging, which is difficult to modify, however it is feasible to postpone photo-aging by adjusting external influences. A healthy diet and well-balanced nutrition are essential factors in delaying aging and extending life [2].

Lipid peroxidation, DNA damage, and inflammation are the fundamental causes of skin aging, illness, and malfunction, according to the free radical hypothesis. As a result, a medical revolution centered on antioxidants and free radical scavengers for skin aging prevention and therapy. Oxygen-free radicals are present throughout the cell metabolism process and can interact with DNA, proteins, and polyunsaturated fatty acids in the body, resulting in DNA breaks, oxidative damage, protein–protein cross-linking, protein–DNA cross-linking, and lipid metabolism oxidation, among other things. ROS has been linked to a variety of cardiovascular illnesses, malignancies, and the aging process. Exogenous antioxidant supplements, with food as a major source, have become a study issue since in vivo oxidation ultimately leads to organism aging [2].

The R&D cycle for novel therapies confronts a number of obstacles, including high cost-to-market, low clinical trial success, and protracted cycle lengths. Despite record expenditures, the pharmaceutical industry's productivity of drug R&D remains on the decline.

This tendency may be attributed to a variety of factors, including present market saturation, challenges in getting innovative chemical substances through a rigorous approvals procedure, and willingness-to-pay in established and emerging markets, to name a few. We'll focus on a key obstacle in medicinal chemistry in this section: the intrinsic difficulty of transitioning the drug development process from fundamental research to early clinical trials [3].

Scientists now have more information than ever before on a broad variety of important issues, considerably surpassing the capabilities of most individuals to appropriately interpret and incorporate it into their own workflows and research aims. One solution is to "delegate" our thinking to ai technology when it comes to data integration and diverse data processing. Machine learning and domain-specific ("weak") artificial intelligence (AI) present novel opportunities for small-molecule drug discovery in this context.

Machine learning systems that may be classified as weak AI have achieved significant improvements in both their underlying algorithms and applications. As a consequence, while there is presently no "strong" (universal) AI, we shall use the word "AI" as a synonym for certain machine learning approaches. As a consequence, the focus of this study will be on components of this potential sector that have already shown their utility and application, as well as the technologies that look to be the most promising for the next phase of AI in drug development [3].

B. An Overview of Artificial Intelligence and Drug Development

In 1956, during the Dartmouth Conference, John McCarthy invented the phrase "artificial intelligence" to characterize "the science and engineering of creating intelligent machines." AI is a multidisciplinary discipline that combines information from several domains such as computer programming, math, biology, languages, philosophy, neuro-science, artificial cognitive science, and others. Recent intellectual and technical advancements have facilitated the field's growth from solely theoretical research to the deployment of intelligent systems that address issues in a range of areas. Despite the wide variety of issues that AI can solve, several basic approaches, such as information acquisition and maintenance, knowledge representation, solution search, logic reasoning, and machine learning, are essential in all circumstances [4].

Alan Turing proposed the concept of a Turing Machine in the 1930s, which could simulate computers. Optimisation was at the heart of the early heydey, in the 1950s and 1960s. Symbolic techniques for semantic processing were introduced at this period, as were the notions of logical reasoning and heuristic searching, and man-machine interaction. STUDENT, a 1964 machine that could execute machine proofs of some mathematical concepts and logical reasoning of propositions, was one of the first computers with rudimentary intelligence. ELIZA (1966), a computer that could, although in a limited fashion, replicate human communication, was another early example. The quick creation of these and other AI examples generated a frenzy, culminating in a cycle of unreasonable enthusiasm followed by disillusionment in AI's capabilities. The first "AI winter" was named after the subsequent cooling of such views. Importantly, and AI advocates past and present should be aware of this, AI is based on probability and statistics, whose correct applications are reliant on mathematics, the availability of relevant data, and the capabilities of our technology [5].

Artificial intelligence achieved its second peak in the early 1980s.Two AI-related scientific models, the multilayered feed-forward neural net and the back - propagation algorithm algorithm, have made great progress.These tools enable the creation of an abstract model of the world as well as the updating of the model based on input (learning from feedback). This combination was the first to defeat a human chess player, and it paved the way for a lot of later research in the topic [6].

The forecasting of conformations from protein sequence information was the first use of such methods in chemistry and molecular genetics. Simultaneously, a slew of expert systems hit the market. Carnegie Mellon University, for example, had developed an expert system for the DEC Company. DEC is said to have saved $40 million each year because to this expert system's automatic decision-making. This accomplishment spurred several nations, particularly Japan and the United States, to spend extensively in the creation of 5th computers, sometimes known as "AI computers." Their inability to learn computer algorithms from data and resolve confusion in thinking, on the other hand, was a clear disadvantage. Moreover, the rising cost of maintenance of intelligent systems, blended with the introduction of less costly and speedier computers originally developed by Apple and IBM, ended up causing the market for such systems to come crashing down, heralding AI into a cold season with hardly any hope of re-emerging into the mass market [7].

Despite its removal from public view and a corresponding reduction in funding, work on such issues did not come to a halt. Improvements focused on increasing the statistical validity of AI models' reasoning. A new paradigm, machine learning, placed a strong emphasis on extracting actionable insights from complex data, which sparked interest in the scientific community as a whole.

Assumption, Bayesian networks, support vector machines (SVM), and decision trees were among the innovative algorithms and approaches described.Expert systems were overtly "conditioned," whereas machine learning models are "trained" to discover patterns in data. Predicting whether molecular properties of a collection of chemical structures are associated to a given set of biological consequences and extrapolating new territory from such descriptions, for example, if a molecule is likely to produce severe toxicity, is one instance. In certain aspects, this idea allows for the automating of much of the quantitative structure–activity relationship (QSAR) modeling work done in the area of cheminformatics [8].

The present AI boom started in the half of the 20th centuries, pushed by the fast development of stored data ("big data"), a simultaneous surge in computer capacity (GPUs, Google's tensor processing units (TPUs), and continual algorithms improvement, such as deep learning. For the first time, we can train nontrivial combinations of network parts on enormous quantities of data in a reasonable amount of time, boosting the applicability of such models. In sectors as varied as e-commerce, games (e.g., AlphaGo, Poker, and DOTA2), medical image analysis, and self-driving cars, the ability to train deep hierarchical network models in a decent length of time has proved the extraordinary possibilities of such techniques [9].

While AI is not new, its application to drug discovery, particularly in modeling generalized structure–activity relationships, is. Actually, the use of experiment data and a "descriptor set" for correlation goes all the way back to (and conceivably even before) Hammett's innovative equation linking reaction rates and equilibrium constants for interactions of benzene derivatives and Hansch's machine detection and characterization of physicochemical characteristics of biologically active compounds, who is generally regarded as the "father of QSAR" in the drug sector [10].

Ever since, a growing number of medicinal chemists have turned to artificial intelligence (AI) to help them evaluate and anticipate chemical biological functions. For instance, pattern recognition focuses on clarifying and analysing patterns shared by chemical entities, based on general premise that substances with similar structural arrangements should have comparable physical qualities and in vitro biological actions. Early neural network designs and applications (for example, the Perceptron and its enhanced versions) appeared, promising to overcome such difficulties. Around 1990, neural networks started to have an influence on the pharmaceutical business due to their usability as pattern matching engines [11].

Weinstein et al. published a paper in 1992 in which they created neural networks to anticipate the mechanisms of action in a cancer medication screening program. The first automation molecular design approach based on neural networks and algorithms was reported in 1994. These integrated learning and decision-making models are the first functional machine learning models, and they possess all features of AI, such as the capacity to I solve problems, (ii) learn and adapt, and (iii) deal with new circumstances [12].

A variety of machine learning techniques have been created and deployed to drug design to assist bridge the gap between serendipity-based and rational drug design, in addition to the aspects mentioned in the preceding section. They

all confront the same difficulty in some way: choosing which biological traits should be combined to collect the information that may lead to the most accurate estimations [13].

More competent ways were needed, which supported the creation of contemporary deep learning, which became a more solid idea about 2010 after individual advancements in the 1990s. The capacity of certain deep learning approaches to investigate and anticipate intricate correlations between molecular representations and observations (bioactivity, toxicity, and so on) gives reason to be optimistic that these methods will provide more meaningful, generalizable insights [14].

These techniques won the Kaggle competition for chemical activity forecasting in 2012 and the NIH Tox21 challenge for toxicity prediction in 2014, both of which were regarded as difficult, and they performed as good as or better than the best methods available at the time.Several large-scale agreements between top pharma and AI businesses have been revealed in recent years, indicating that pharmaceutical corporations that traditionally stood on the sidelines of contemporary AI are suddenly joining in [15].

C. Artificial Intelligence Applications in Drug Research

Algorithms for artificial intelligence are a vast area that encompasses a wide range of techniques. To help readers better grasp AI-assisted drug development, we will present a quick review of the main concepts of those algorithms that are extensively utilized in drug discovery.

The seven kinds of learning functions and methodologies utilized in drug discovery projects include supervised, unsupervised, semisupervised, active, reinforcement, transfer, and multitask learning. Every class has its own set of benefits and drawbacks. The job at hand should dictate the technique of choosing [3].

1) Supervised Learning

A supervised learning process is used by many AI learning algorithms, in which a set of input data and known responses to the data are required, and the aim of this newtechnique is to understand a mapping function from the input to the output:, such that the class labels Y or target values Y for unseen supervised learning approaches include all categorization and regression algorithms [16].

2) Unsupervised Learning

When just input data (X) and no matching output variables are available, unsupervised learning techniques are utilized. In other words, the data is unlabeled in an unsupervised model. It's tough to come up with a relevant performance statistic for the algorithm in this situation. Instead, the algorithm will extract structures (= features) from the data (= patterns) that may be utilized to categorize the input samples into groups. Unsupervised learning algorithms are used in tasks like computation and dimension reduction, for example. Unsupervised learning contrasts with supervised learning in that it does not employ a feedback signal to assess the quality of feasible alternatives. Unsupervised learning methods such as clustering and projection are two common examples [17].

3) Semisupervised Learning

Semisupervised learning lies at the intersection of supervised and unsupervised learning methodologies, and may be effective when there are a lot of input data (X) but just a few labeled examples (Y). This category encompasses a large number of real-world drug discovery issues. Semisupervised learning may make the most of unlabeled data by modifying or reprioritizing predictions derived just from limited labeled data. This is commonly achieved by training a model with the available labeled data using a supervised learning method, using the trained model to predict labels for the unlabeled data using the trained model; and, retraining the model with the quasi samples and the labeled data.In this method, the original labeled sample distributions are utilized to create the model and possibly improve its prediction capacity with minimal extra real-world, e.g., practical experimental, cost [18].

4) Active Learning

Active learning is a particular variant of semisupervised learning that takes a different approach to the problem of inadequate labeled training data.

In this situation, the user (or another source of data) may be asked to provide labels for data sets in the input space areas where the algorithm is least confident. Active learning seeks to reduce the number of labeled examples necessary for learning at the same time, rather than seeking to utilize the underlying structure of data sets with the explicit objective of improving label predictions [19].

5) Reinforcement Learning

Reinforcement learning aspires to be similar to incentive learning in certain ways. In its most basic form, an agent tries to identify the best set of actions to achieve a certain goal. This aim is achieved by assessing the environment, taking actions to change the environment (using policies to convert the agent's internal state into actions), and rating the results of those activities (reward). This pattern of effective penalties and rewards enables us to create and develop systems without necessarily understanding the "right" or "ideal" strategy, as long as reward function success corresponds pretty well with objective success [20].

6) Transfer Learning

The phrase "transfer learning" refers to a set of techniques that do away with the constraint that training and validation data be in the same feature set and have the same distribution. As the name indicates, transfer learning approaches learn and transfer useful knowledge from old information domains to a new data domain, with the purpose of enhancing anticipated performance on the target domain if accomplished [21].

7) Multitask Learning

In past few years, another learning technique, multitask learning, has gained increasing popularity of drug discovery. Rather of learning just one task at a time, as is the case with single-task learning, multiple separate but significantly associated tasks are acquired in parallel and are attempted to share an underlying structure. When it comes to presuming multitarget prediction models, this notion is extremely intriguing. Although multitasking and transfer learning are similar, they vary in how they approach the tasks at hand, with multitasking assuming task equality and learning techniques assuming a well-defined imbalance [22].

METHODOLOGY

A literature search was conducted using the keywordsin PubMed: "deep learning antioxidant", "algorithms antioxidant", "neural networks antioxidant", "support vector machine antioxidant", "natural language processing antioxidant", "computer vision antioxidant", "artificial intelligence antioxidant", and "machine learning antioxidant".

There were a total of 146 papers chosen for evaluation.This research only looked at full-text papers that were available for free. The relevance of the abstracts was determined, and 29 publications were judged to be relevant to the current study.Relevant references were examined in bibliographies, as well as headlines relating to the issue.

RESULTS

A. Machine Learning

Zuvuela at al established quantitative structure-activity relationships models for flavonoids' oxygen radical absorbance capacity prediction. The criteria of two well-known antioxidant activity mechanisms, the hydrogen atom transfer (HAT) mechanism defined by the minimum bond dissociation enthalpy and the sequenced proton-loss electron transfer (SPLET) mechanism defined by proton affinity and electron transfer enthalpy, were used to construct both linear (PLS) and non-linear (ANNs) models. The results of the ANN-based QSAR simulations are consistent with the findings. Finally, a series of 115 flavonoids were created combinatorially employing flavone as a template, and the highly predictive ANN-QSAR model was utilized to predict antioxidant activities [23].

Shen et al presented AOP-HMM, a computational model that extracts selective evolutionary characteristics from hidden Markov model (HMM) profiles to predict antioxidant proteins. The HMM profiles were first transformed into fixed-length feature vectors using auto cross-covariance (ACC) variables. Then, to decrease the dimensionality of the raw feature space, they used the analysis of variance (ANOVA) approach. Finally, a support vector machine (SVM) classifier was used to predict AOPs. AOP-HMM outperformed the majority of current approaches in the trials, demonstrating that it may be used to swiftly annotate AOPs and steer the experimental process [24].

DrugAge (http://genomics.senescence.info/drugs/) is a curated library of medications and substances that may help people live longer lives. DrugAge now has 1316 entries with 418 distinct chemicals from investigations in 27 different model species, including worms, flies, yeast, and mice. 324 papers were manually selected for data. A functional enrichment study of targets of lifespan-extending medicines were run using drug-gene interaction data. Functional categories relating to glutathione and antioxidant properties, intracellular transport, and metabolic functions are among the enriched phrases. DrugAge is a free online resource for scientists and will be a valuable resource for biogerontologists [25].

SeqSVM is a computational technique for predicting antioxidant proteins based on their basic sequence properties. By using the max relevance max distance approach, the features are deleted to decrease duplication. Finally, antioxidant proteins are identified using a support vector machine (SVM). The results of the experiments showed that the technique outperforms current methods, with an overall accuracy of 89.46 percent. Although the suggested computational method

achieves a promising classification result, the experimental findings are confirmed using biochemical methods such as wet biochemistry and molecular biology [26].

Garcia-Perez et al. reported on the research of phytocompounds in Bryophyllum sp., the application of plant tissue culture methods as a reliable instrument for the valuation of bioactive chemicals, and the use of machine learning techniques to model and maximize Bryophyllum spentire .'s phytochemical potential. Bryophyllum species may be a prospective source of plant bioactive chemicals with high antioxidant and anticancer potential, which might be exploited in cosmetic, food, and pharmaceutical sectors on a big scale [27].

Chen et al. designed quantitative structure-activity relationship (QSAR) models based on 91 antioxidant tripeptides. They used the stepwise regression (SWR) method to select critical variables without autocorrelation, and then developed predictive QSAR models based on the screened variables using multiple linear regression, support vector machine, random forest, and partial least square regression.19 antioxidant tripeptides were generated using SWR-MLR models, and their antioxidant activity in free radical systems was tested using three antioxidant tests.The developed QSAR models may be utilized to find and test new high-activity antioxidant tripeptides [28].

ANPrAod is a model that may be used to find antioxidant proteins. Xi et al computed 673 amino acid reduction alphabets to identify the best feature representation method in order to minimize possibly duplicate features and increase prediction accuracy. The resulting model had a five-fold cross-validation accuracy of 87.53 percent and a ROC of 0.7266, which was better than the prior techniques. The findings of the independent dataset further revealed ANPrAod's good resilience and dependability, suggesting that it might be a useful tool for identifying antioxidant proteins and contributing to hypothesis-driven experimental design [29].

Ho Thanh Lam et al created a machine learning-based model for prediction of antioxidant proteins. The studies were carried out using 10-fold cross-validation on the training process, and three separate independent datasets were used to verify the results. On an ideal collection of sequence characteristics, several machine learning and deep learning techniques were assessed. Random Forest was shown to be the best model for identifying antioxidant proteins with the greatest performance among them. On the training dataset, the optimum model identified antioxidant proteins with an accuracy of 84.6 percent and a balance of sensitivity (81.5 percent) and specificity (85.1 percent). The importance of this approach was further shown by the performance findings from several independent datasets when compared to previously published efforts on antioxidant protein identification [30].

The Antioxidant Database (AOD) was created to aid researchers in understanding and revealing the biological roles of antioxidant proteins. The AOD database may be found at http://lin.uestc.edu.cn/AODdatabase/index.aspx. AOD currently has 710 antioxidant proteins in its current release. AOD extracts categorization, source organism, subcellular localization, gene products, catalytic properties, and functionality of antioxidant proteins from UniProtKB/Swiss-Prot. In addition, AOD now includes two web-based tools for doing sequence similarity searches and computationally identifying antioxidants [31].

In the context of a biomarker selectively produced by lipid peroxidation (a result of oxidative stress), such as F2-isoprostanes, Idowu et al developed an AI-based machine learning (ML) model to link a polyphenol's antioxidant action as an output variable to molecular descriptors (factors governing in vivo antioxidant activity) as input variables. Support vector machines, artificial neural networks, and Bayesian probabilistic learning are some of the main approaches that might be applied. This model will be a solid predictor of biorelevant antioxidant capacity of polyphenols, making antioxidant compound identification and design simpler. The method will also help to satisfy the 3Rs criteria when using animals in scientific research (replacement, reduction, and refining) [32].

IDAod is a user-friendly web server for antioxidant protein identification and can be found at http://bigroup.uestc.edu.cn/IDAod/. Based on a mixed g-gap dipeptide component feature vector, Shao et al developed a deep learning-based classifier to detect antioxidant proteins. To extract nonlinear model from raw input, the classifier employs a deep autoencoder. To minimize dimensionality, the t-Distributed Stochastic Neighbor Embedding (t-SNE) method was applied. Lastly, the data was classified using a support vector machine. In 10-fold cross validation, the classifier received a F 1 score of 0.8842 and an MCC of 0.7409. Their suggested technique outperformed standard machine learning methods in experiments, indicating that it might be a useful tool for identifying antioxidant proteins [33].

Bai et al used the Tox21 challenge dataset to build and validate a series of predictive models that used deep learning algorithms like deep neural networks, convolution neural networks, recurrent neural networks, and highway networks to determine whether the compounds are ARE activators or inactivators. With accuracy of 0.992, 0.914, and 0.917 for the training set, test set, and validation set, respectively, the DNN prediction model based on fingerprint characteristics has

the best prediction ability. As a result, these robust models may be used to predict the ARE response of molecules quickly and precisely, which is critical for assessing the safety of drugs throughout the drug discovery and development process [34].

A new dataset was built by Guardado et al utilizing databases that gather the flavonoid content of various foods. A structural-topological technique termed TOPological Sub-Structural Molecular Analysis was used to collect structural information (TOPSMODE). Various artificial intelligence techniques, including Machine Learning (ML) methodologies, were used. Using structural-topological features of dietary flavonoids, they were able to show the efficacy of the models. Except for the Multi-Layer Perceptron (MLP) technique, the models presented may be regarded successful in estimating new values of Oxygen Radical Absorption Capacity (ORAC) without generalization. The Random Forest (RF) method produced the most ideal model. By incorporating new structural-topological qualities and choosing those that most impact the class variable, the in silico approach they devised enabled them to validate the usefulness of the produced models [35].

Using large and diverse pharmacological and natural chemical data, Yoo et al created a deep learning-based strategy for identifying the therapeutic applications of natural compounds. Deep learning can efficiently use heterogeneous characteristics to relieve incomplete information, which is the motivation for this technique. They produced 686 dimensional characteristics for 4,507 natural chemicals and 2,882 authorized and experimental pharmaceuticals based on latent knowledge, molecular interactions, and chemical property aspects. The produced features and confirmed pharmacological indication data were used to train the deep learning model. Potential efficacies were accurately predicted with high sensitivity, specificity, and accuracy when natural compound characteristics were used as inputs to the trained model [36].

AOPs-SVM is a model based on sequence characteristics and a support vector machine that was constructed using machine-learning methods. The creators ran a jackknife cross-validation test using the suggested AOPs-SVM classifier using a testing dataset and got 0.68 in sensitivity, 0.985 in specificity, 0.942 in average accuracy, 0.741 in MCC, and 0.832 in AUC. Existing classifiers were outperformed by this. The findings of the experiment show that the AOPs-SVM is a useful classifier that adds to antioxidant protein research. To allow open access, a web server was established at http://server.malab.cn/AOPs-SVM/index.jsp [37].

Kennedy et al identified peptide RTE62G (pep RTE62G), a naturally occurring, unaltered peptide with ECM modulatory properties, using an artificial intelligence (AI) technique.In vitro, vivo, and proof of concepts clinical trials were used to evaluate pep RTE62AI-predicted G's anti-aging capabilities. Pep RTE62G was extracted from a plant source, Pisum sativum, using a deep learning approach (pea).The in vitro impact of pep RTE62G was next assessed using human dermal fibroblasts (HDFs) and keratinocytes (HaCaTs) cell culture assays. ELISA tests were used to assess various activities such as cell proliferation and ECM protein production properties. A wound healing assay was used to measure cell migration, while immunofluorescence imaging and PCR were used to study ECM protein synthesis and gene expression, respectively.To investigate the induction of ECM proteins by pep RTE62G ex vivo, immunohistochemistry was used on human skin explants. Finally, the clinical efficacy of pep RTE626 was assessed in a 28-day proof-of-concept pilot study [38, 39].

Pep RTE62G is an effective multi-functional anti-aging ingredient, according to in vitro testing. In HaCaTs, Pep RTE62G administration promotes both cellular proliferation and migration. Pep RTE62G also reliably stimulated the neosynthesis of the ECM proteins elastin and collagen in HDFs, which was verified in human skin explants. Finally, pep RTE626 shown anti-wrinkle and collagen stimulatory potential during a 28-day period in our proof-of-concept clinical research.pep RTE62G is a pure, unmodified peptide with anti-aging properties predicted by AI and experimentally validated [39].

With a focus on peptides, Doherty et al. proposed for complementing, if not replacing, the conventional sequence of functional food ingredients (FFI) structural characterization with an AI-powered solution by integrating AI at the start of the process. To describe functional food components, in silico bioinformatics, in vitro, and HTP screening approaches have substantially enhanced the procedure (FFIs). Bioinformatic tools that perform similarity searches, such as the Basic Local Alignment Search Tool, may be used to mine proteomes in silico (BLAST).These methods, on the other hand, usually analyze and extrapolate on previously collected data and are unable to anticipate molecular entities and functions from scratch.

Artificial intelligence (AI) methods, particularly deep learning approaches, could and should be used to speed up de novo algorithmic identification of bioactive components and their functions, resulting in true innovation at an unprecedented speed in areas like functional ingredients and small molecules, and providing novel insights for a variety

of questions. In other words, AI shifts the paradigm away from screening and retroactive benefit assignment and towards design based on predefined benefits [40].

Bioactive peptides derived from food have fantastic potential in treating and maintenance of a variety of health conditions, including chronic inflammation. A rice-derived functional component termed a natural peptide network (NPN) significantly reduced Tumour Necrosis Factor (TNF) production in human macrophages in vitro in response to lipopolysaccharides. Rice NPNs were characterized using AI, and liquid chromatography tandem mass spectrometry was utilized to confirm the presence of seven potentially active peptides.In vitro, the anti-inflammatory capabilities of the network's component peptides were confirmed [40].

To forecast whether a chemical substance would lengthen the lifespan of Caenorhabditis worms, Kapsiani et al created a machine learning technique based on information from the DrugAge database. Chemical fingerprints and molecular descriptors were employed as features in five prediction models built using the random forest technique. For classifying the substances in the test set, the top-performing classifier, which was created using molecular descriptors, obtained an area under the curve score (AUC) of 0.815.The Gini significance measure of the random forest technique was used to rank the model's features. Atom and bond count descriptors, as well as topological and partial charge features, were among the top 30 traits. In an external database of 1738 small compounds, the model was utilized to predict the substance. In the screening database, chemical compounds with a prediction probability of 0.80 for increasing Caenorhabditis elegans longevity were classified as (1) flavonoids, (2) fatty acids and conjugates, and (3) organooxygen compounds [41].

Deep learning is used in the AnOxPePred program and web-server to predict the antioxidant properties of peptides. Olsen et al's model was trained using an experimentally tested dataset of antioxidant and non-antioxidant peptides. This technique outperforms a k-NN sequence identity-based approach in prediction on a range of measures. In addition, the new approach will serve as a suitable standard for future antioxidant peptide predictors. The tool is available at http://services.bioinformatics.dtu.dk/service.php?AnOxPePred-1.0 [42].

B. Artificial Neural Networks

Ferulic acid ester has been shown to be more efficient in treating several clinical conditions and reducing lipid oxidation.To model and improve the solvent-free and low pressure water evaporation in the lipase-catalyzed synthesis of 2-ethylhexyl ferulate (2-EF) from ferulic acid and 2-ethylhexanol, a Box-Behnken design integrating response surface methodology (RSM) and artificial neural network (ANN) was used. ANN surpassed RSM in data fitting based on residual values and coefficient of determination (R2) obtained from the design data. Overall, in a reduced pressure evaporation environment, the current lipase-catalyzed 2-EF synthesis technique yields a high yield of 2-EF at low reaction temperature. This technique, in particular, has the potential to reduce enzyme denaturation and ferulic acid oxidation, two prominent side effects of long-term biosynthetic activity at high temperatures [43].

Liu et al extracted Rosa sterilis flavonoids using an ultrasonic technique, and the extraction conditions were modeled and adjusted using response the surface approach and artificial intelligence. The findings reveal that the ultrasonic approach can successfully extract total flavonoids, and the extraction rate is near to the ANN-GA algorithm's forecast value, demonstrating the model's logic. Material liquid ratio > extraction power > extraction duration > ethanol concentration were the factors that had the most impact on the experiment. Furthermore, the scavenging effects of flavonoids on DPPH, O2-, and OH were investigated, indicating that flavonoids have potent antioxidant properties. Using the data from the extraction process, the kinetics of the extraction process was investigated, and it was discovered that the extraction process followed Fick's first law [44].

Using Artificial Neural Networks (ANNs) technology, Golpour et al investigated the total phenolic compounds and antioxidant activity of strawberries under various experimental extraction circumstances. The trial data was used to train ANNs utilizing Levenberg-Marquardt (LM) and Bayesian Regulation techniques to feed- and cascade-forward backpropagation models. Total phenolic compounds, DPPH, and ABTS antioxidant activity were employed as ANN outputs, while three independent variables (solvent concentration, volume/mass ratio, and extraction duration) were used as ANN inputs. The 3-9-1, 3-4-4-1, and 3-13-10-1 structures, with the learning algorithms of trainlm, trainbr, trainlm, and threshold functions of tansig-purelin, tansig-tansig-tansig, and purelin-tansig-tansig, respectively, were the best cascade- and feed-forward backpropagation topologies of ANNs for the estimation of total phenolic compounds, DPPH, and AB. The best R2 values were 0.9806 (MSE = 0.0047), 0.9651 (MSE = 0.0035), and 0.9756 (MSE = 0.00286, respectively, for total phenolic compounds, DPPH, and ABTS antioxidant activity factors. According to the ANN comparison results, the cascade-forward backpropagation network beat the feed-forward backpropagation network in predicting TPC, whereas the FFBP network outperformed the cascade-forward backpropagation system in predicting DPPH and ABTS antioxidant activity parameters. The artificial neural network (ANN) technology can be used to estimate total phenolic compounds and antioxidant activity in strawberries [45].

CONCLUSION

To summarize, AI has the potential to help in a variety of antioxidant identification discovery fields. As with any concept, it is unlikely to be a panacea, but its use should be expanded to help scientists in their various roles and specialties throughout the process. Domain-specific AI applications in industry are just getting started. We are unlikely to see seismic changes overnight; as supplement discovery remains a slow business based on risk management and the development of novel science within the constraints of patient and shareholder responsibility.

However, combining these approaches has the potential to significantly increase efficiency in some parts of the pipeline, giving researchers more time to focus on different problems by offloading simple tasks to AI and robotics combinations. Furthermore, AI provides potentially useful insights to seasoned scientists through its extensive "working memory," which is essentially a new perspective. Nonetheless, there will be setbacks and duplications of effort in the process of implementing these changes. We are confident, however, that AI will alter certain drug discovery processes and advance innovative bioactives research and development.

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