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Role of artificial intelligence in chemistry

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ABSTRACT

Recently, artificial intelligence is one of the most cited areas in chemistry. Chemistry and Artificial Intelligence are inextricably linked! Artificial Intelligence and Chemistry applications in the healthcare industry are mostly focused on drug discovery and development. With the integration of technology and medicine, drug formulation and production has evolved significantly. Due to the technologically complex technology and equipment employed by scientists, this method has also been a product of improved research and development in the pharmaceutical business. However, the application of artificial intelligence in chemistry is not limited to drug development. It goes beyond molecules and chemical bond building blocks, which are the foundations of science. When it comes to chemistry and related areas, AI can help with everything from molecule synthesis to molecular property identification. In this review article, we tried to provide an overview on how AI assists researchers and scientists in demonstrating their usefulness and applicability in drug developments and delivery processes.

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1. Introduction

John Mc Carthy was the first who coined the term artificial intelligence in 1956. Artificial intelligence is the branch of computer science that deals with the machine learning process, which can perform different tasks that typically require human intelligence. Perhaps artificial intelligence is the replication of human intelligence in the machine [1]. It is an essential part of the technology industry because it helps collect and analyze data at a low cost and safe working environment [2]. Artificial intelligence has many applications, such as natural language processing, reasoning problems, making strategies, etc. It can modify the objects based on its requirement [1]. Artificial intelligence is helpful in the engineering field and has many applications in the chemical field. It is helpful to design a molecule and predict its various properties like melting point, solubility, stability, HOMO/LUMO, etc [3]. Artificial intelligence is also helpful in drug discovery and structure determination in less time, which is also cost-effective. Many chemists used artificial intelligence to determine the effect of chemicals and were also helpful in determining the structural patterns of different molecules.

As we know, the whole world is suffering from coronavirus, so this artificial intelligence and COVID- 19 sensors help examine the structure of coronavirus, its life cycle, infection pathways, and functional sites that are useful for therapeutics discovery and pathogenesis. The combination of artificial technology and IoT (internet of things) is used to fight against SARS-COV-2. Peoples have smartphones, so during lockdown during COVID- 19, an artificial intelligence system is used to share national policies and educate people about COVID- 19 to regulate national protocols and share health data properly [4].

This artificial intelligence system is significantly less time-consuming and provides an output within a lesser period based on input given by someone. This machine-based software can also help in solving various other problems related to chemistry [5]. The Fig. 1 shows the various applications of artificial intelligence in different field of chemistry. The first and foremost application of AI in chemistry is the prediction of molecular properties. Detection of molecular properties has enabled the scientist to evaluate the potential of hypothetical molecules. Along with this, use of artificial intelligence in molecular design has triggered revolutionary discoveries in the field of chemistry. Other topmost applications of artificial intelligence in chemistry are the process of drug discovery, reterosynthetic reactions, predictive analysis, nanotechnology, waste water treatment etc.

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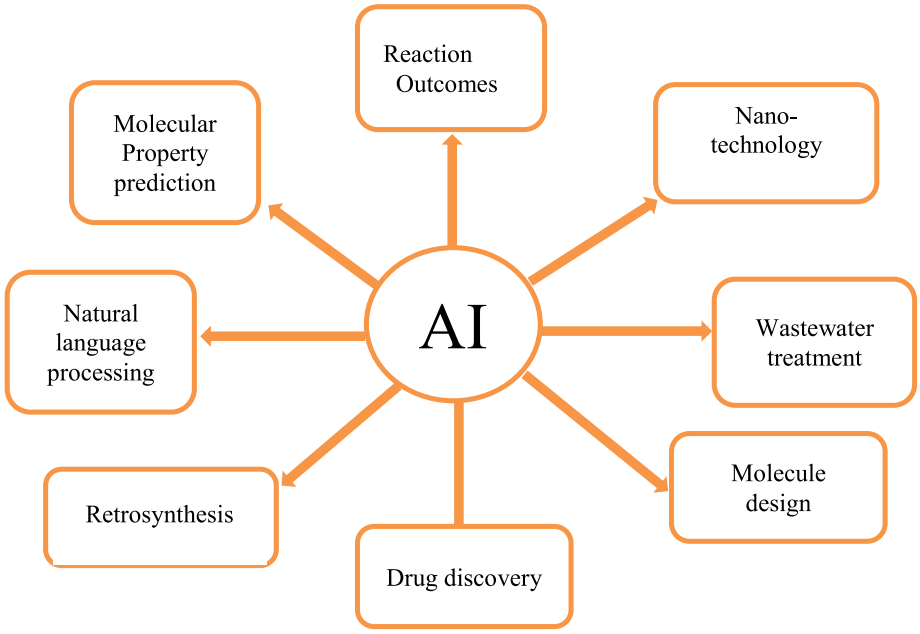

Fig. 1. Various applications of artificial intelligence in the field of chemistry.

The drug discovery process is demanding in day-to-day life, but the rate of this process is low because of its multi-objective nature. Artificial intelligence is useful in drug discovery by using the previously available data set. Artificial intelligence-based algorithms are instrumental in making a drug from a large complex molecule, while manually, making a drug is very difficult [6]. This is also helpful in uncovering the hidden patterns of large complex molecules. Artificial intelligence also contains many algorithms that are useful in designing a new molecule and finding out the active site in a drug [7]. Artificial intelligence provides a large amount of data set that is useful in identifying the patterns between the training set and control internal and calculating new patterns. This feature of machine learning helps in determining the materials [8]. Artificial intelligence is also an essential part of many applications like in our day-to-day life. We use Google, Siri, and Alexa to search for something and talk to Siri and Alexa voice assistant recently used to perform quantum chemistry calculations [9].

As we know, the synthesis of an organic molecule is the most crucial task in organic chemistry. For the synthesis purpose, scientists used this computer-aided software for many years. For new product generation, a large amount of data set based on artificial intelligence is used by a scientist in which starting material is known, and only focus is on the target molecule. Combining artificial intelligence with biology is helpful to synthesize a new molecule that will be useful to cure a disease [10]. Some machine learning methods combined with active learning are naturally similar to the concept of response loops. Active learning is the process of intelligently searching the problem and provide an efficient path for this problem [11]. Based on the goals and data available, all types of artificial intelligence may find applicability in chemistry. Artificial intelligence has many powerful tools that are sufficient to solve and tackle chemistry problems. Artificial intelligence is helpful to identify the patterns and correlations in data and provide solutions to any problems. Artificial intelligence can also provide the reaction outcomes from the previously available data [12].

Artificial intelligence is also playing an essential role in retrosynthesis. The Retrosynthesis process starts from the target molecule and continues until getting the starting precursors of that molecule, and with the help of this simple precursor, it is possible to synthesize a new molecule [13]. Artificial intelligence is also valuable for waste-water treatment. This technique implements some algorithms for the waste-water treatment plant to make the analysis more intelligible and remove pollutants from water [14]. Combining artificial intelligence with nanotechnology provides new tools for information and communication technology that significantly impacts our society [15].

This review work is carried out mainly to provide information about artificial intelligence, which can be used in chemistry. Artificial intelligence is used in our daily life, and it became an essential part of our daily life. This review paper focuses mainly on the use of artificial intelligence in chemistry. Chemists can explore their knowledge by using artificial intelligence. Artificial intelligence can help to reduce time and is also cost-effective. Many pharmaceutical industries use AI in drug development. This review focuses on various applications of artificial intelligence in chemistry like retrosynthesis, drug discovery, reaction outcomes prediction, etc. This review article also tells us about the use of AI in nanotechnology and waste-water treatment.

2. Literature review

2.1. Artificial intelligence in retrosynthesis

The planning and synthesis of a molecule is a crucial task in organic chemistry. It includes Complexity in molecules various steps with the help of which an organic molecule can be synthesized. For this purpose, retrosynthesis is used. Retrosynthesis is a technique in which a target molecule is transformed into a simple precursor. This process is continued until the starting molecule is obtained [16]. However, if the molecule is very complex and contains many functional groups, it is challenging to synthesize it [17]. For example, Herculean B has 32 stereocentres and synthesis of this molecule required 47 reactions. The synthesis of complex molecules always remains a challenging retrosynthetic problem. Nevertheless, with the help of artificial intelligence-based

algorithms, it is possible to overcome the complexity of this molecule. This algorithm aims to provide a reaction path to the target molecules to convert into a simple precursor [18]. Chemists use artificial intelligence to perform retrosynthesis analysis and can explore their knowledge [19]. The chemical literature has been grown increasingly, so it is complicated to manage the decision-making process. However, it is thanks to a network of organic chemistry, which contains all the reactions published in the literature [18].

Unlike contemporary times when scientists take the help of AI to conduct retrosynthesis reactions (Fig. 2), scientists in the past used to conduct this process manually. This process was an extensive experience as it demanded a lot of time and resources. However, with the coming of AI, this process can beconducted with the help of computers that have made it more accurate and efficient at the same time.

The retrosynthesis used some reaction rules that contain a set of transformations. Some expert chemists have encoded this rule [21]. This reaction rule represents the generic reaction applied to the target molecule to generate a simple precursor. Once the rule has been finalized, the algorithm used a matrix to determine the rules for each step of the reaction. The artificial intelligence used the Monte Carlo tree with three neural networks that help in selecting the candidate reaction for expression. This neural network has been trained in such a way so that they can select a reaction center [18]. However, this rule-based approach is not efficient for the molecule beyond the transformation rule's scope. To overcome this problem, a new approach that is known as deep learning has been introduced. The advantage of this approach is that it can extract the generalized patterns from a large amount of available data set. In this deep learning approach, the target molecule is encoded and extracted from the SMILE string. These strings have been converted into another set of characters related to the reactant's SMILE string (simplified molecular-input- line-entry system) [21].

2.2. Artificial intelligence in the prediction of reaction outcomes

To synthesize a product, a chemist has to imagine a sequence of possible chemical transformations that could produce the feasible product, based on his/her knowledge and the scientific literature, and then perform the reaction in a laboratory, hoping that they happen as expected and give the desired product.

The expert can easily predict the product of a simple reaction, but it is challenging to predict the product of a significant complex reaction, so here comes the role of artificial intelligence. The large complex molecules can be handled by a trained data set built by artificial intelligence [22]. The artificial- intelligence-based algorithms can be trained with a known set of chemical reactions to predict the outcomes of a reaction with high accuracy [23]. The outcomes of the reaction can be predicted by using two steps: (1) by applying a forward reaction template to the reactant molecule. (2) By finding the reaction product formed in significant amounts by using the machine learning method (Fig. 3). In the first stage, apply the forward synthetic templates library to the initial reactant molecule and determine which product is formed. In the second stage, each of the reactants has been scored by a machine learning model. A function known as the soft-max network layer compares the score of all these reactions and generates a more significant product. For example,

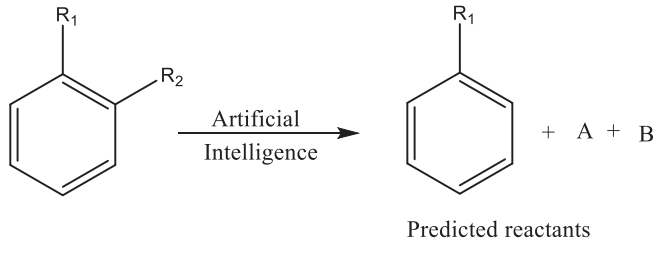

Fig. 2. Retrosynthesis by Artificial Intelligence [20].

$$A + B \rightarrow C$$

The yield of this reaction is 50%, and the reaction with D, E, etc., forms a lesser amount of yield. Thus, the training data set provide more information from each reaction [24].

Artificial intelligence-based methods help recognize the images, bioinformatics, and predict molecule's biological activity and reaction mixture composition. The random forest method is a more precise method used in the reaction outcomes prediction in which its decision tree trains the training set [25].

2.3. Artificial intelligence in molecular designing

Machine learning has found success in recent years in property prediction and the discovery of a material. These machine learning-based tools are helpful in the discovery of molecular patterns, properties, their relationship, and predicting the reaction outcomes. It is also helpful in decreasing the size of the dataset by removing errors. Machine learning helps predict the properties of a molecule without having any knowledge of the chemistry and physics behind this molecule. In addition, when using this kind of algorithms, one should verify that the generated molecules are effectively different from the molecules of the training dataset and measure the chemical diversity of the generated molecules (how different they are from known compounds) as shown in Fig. 4.

Artificial intelligence is also helpful in the organic photovoltaic field (OPV) by predicting the frontier molecular orbitals with the help of a trained neural network. The chemical structure of this molecule has been generated by using 26 basic building blocks, and the data for this molecule has been taken from the Harvard clean energy project. To convert the raw data into machine-readable representation, we required a programing language expression. The original expression can be derived from the image connected with PCE (power conversion efficiency) contains some hidden pattern. Thus, to overcome this problem, we use deep learning to unhide an image's feature [26].

2.4. Artificial intelligence in waste-water treatment

The most critical problem is eutrophication that has been increased day by day because of the increase in the industry. The level of phosphorous and nitrogen in water decrease because of the industrial waste chemicals and products that cause eutrophication. Artificial intelligence is helpful in the treatment of waste-water by taking the data from the biological stage. This data provides a prediction based on the behavior of the bioreactor [27]. The membrane bioreactors are the sustainable technologies that are used in the treatment of waste water. The currently available tools used for adjusting operating parameters are not enough to ensure treated water quality. However, artificial intelligence is helpful in the management of necessary parameters in waste-water treatment. Artificial intelligence is used in membrane bioreactors to control and improve membrane fouling [28]. It provides an operation that is useful in waste-water treatment. A waste-water treatment plant has been designed that uses the treatment property of effluents and uses some biological, physical, and chemical properties to treat water pollutants. This artificial intelligence-based system is more efficient than the human understanding in

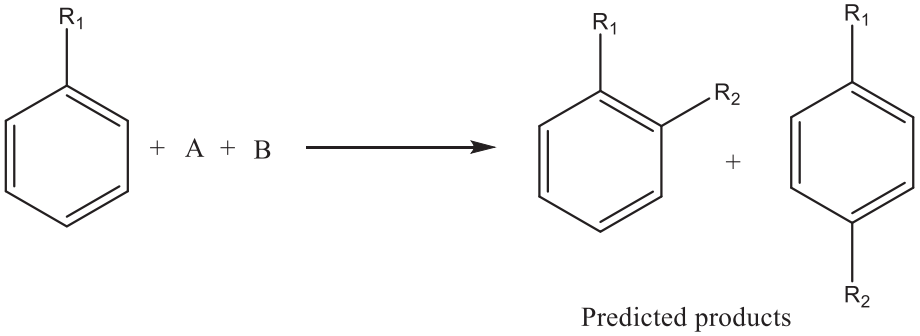

Fig. 3. Reaction outcomes prediction by Artificial Intelligence [20].

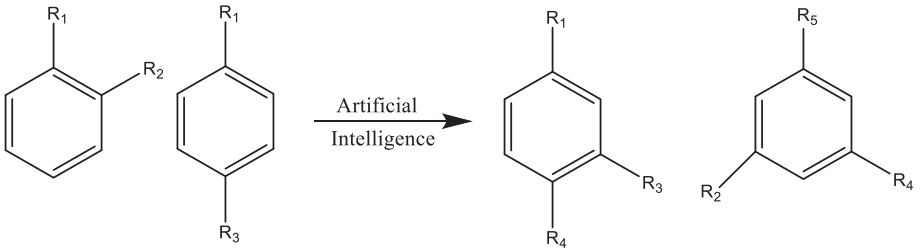

Fig. 4. Molecular designing by Artificial intelligence [20].

the waste-water treatment plant. This technique implements some algorithms for the waste-water treatment plant to make the analysis more intelligible. The activated study model (ASM2d – guided) QL (Q- learning) algorithm contains its self-learning mechanism used to optimize the control strategies like hydraulic retention time and internal recycling ratio for waste-water treatment plant systems. Combining the online learning procedure and the neuro-fuzzy controller is very helpful in controlling a bioreactor (in waste-water)—the Kohonen self-organizes waste-water quality and checks out the harmful component's concentration in the waste water. Artificial neural network algorithms are used in forecasting for the waste-water treatment plant. COD (chemical oxygen demand) is the most critical variable that an expert uses in making decisions based on measuring this variable in biological treatment. The primary purpose of this biological waste-water treatment is to remove the pollutants from the water. COD acts as an indicator of water pollution and is helpful to find out the efficiency of the WWTP process [27].

Artificial intelligence techniques use experimental data to predict, optimize, and conformation contaminant removal in the waste-water treatment process. These experimental data include training, validation, and testing of a molecule. An artificial neural network determines the nitrogen content in waste-water treatment using the contact aeration process. Artificial intelligence is helpful in the recovery of clean water during waste-water treatment. The reuse of waste-water helps to increase the quality of the environment, and water-saving is also increased. For this use, the rainfall water index is an input in the model [29].

2.5. Artificial intelligence in nanotechnology

Artificial intelligence is mainly based on biological things, while nanotechnology combines physics, chemistry, and engineering [30]. So, the combination of artificial intelligence with nanotechnology provides new tools for information and communication technology that greatly impacts our society. The various machine learning process like decision tree, vector machine that has been applied to the association, prediction, data mining in the context of nanotechnology research. Scanning probe microscopy is the most commonly used technique in nanotechnology in which interaction between tip and sample is complicated to understand and involves many parameters. To overcome this problem, we can use the artificial intelligence technique. Combining an artificial neural network (ANN) with a principal component analysis provides simplified input data by de-correlating the data and decreasing independent variables. The ANN is trained with a numerical result that is useful to find out the dielectric constant value. The advantage of this method is that we can find the thickness of the thin-film by knowing the dielectric constant value. ANNs is used to determine the structural properties of nanomaterial like alignment and curvature. The artificial intelligence-based algorithms are used to determine the morphology of the CNT turfs. Thus, the ANN models are sufficient to relate the physical appearance of CNT turfs to Raman features. ANNs are also used in determining the properties of a complex system like a thin film. The different artificial intelligence-based training set has been used in determining the property of this nanomaterial. Artificial intelligence techniques are also used in identifying optical techniques because of the increasing growth of broad-band communication. Artificial intelligence helps to determine the chemical kinetics parameters such as rate constant and concentration of the reactant. By using this, we get a new kinetic curve without solving the differential equation. The genetic algorithms (GA) have been used to study the clusters property of nanoparticles. The combination of genetic algorithms (GA) and DFT calculations help to obtain the equilibrium state. The ANNs is used to find out the splitting tensile strength and water absorption values which contain ZnO_2 and Cr_2O_3 nanoparticles. The main problem of nanoscale that scientists are facing is related to its simulation. It is complicated to obtain an actual optical image on a nanoscale. For this purpose, artificial intelligence has increased the quality of simulations to make them easy to interpret [15]. Artificial intelligence helps sequence the

nucleotide in the translational process of Nanopore. The artificial neural network-based transiting used in Nanopore sequencing provides more than 90% accuracy in sequencing [31].

Nanotechnology has many physical limitations on its working scale, and we also know that the microscopic world is entirely different from physics. So correct interpretation of the result is one of the issues. At this stage, artificial intelligence is used for correct scientific results and in Nano applications [32].

2.6. Artificial intelligence in drug discovery

It is challenging to make a drug with the help of a complex molecule that contains more than 10^{60} molecules. Thus, the drug development process is limited because of the absence of advanced technologies. Artificial intelligence plays a crucial role in the structure validation of the target drug and optimizing the drug's structure [33]. The machine learning model has been trained with various data set of existing molecules. This machine learning model helps to encode the higher dimensional representation such as SMILE strings into lower-dimensional representation. This lower-dimensional representation is again decoded and to form a new molecule with a higher dimensional representation. This model is helpful in the prediction of the active molecule. Merk and co-workers did the very first synthesis and testing with the help of a generative model by taking a set of more than 500,000 bioactive molecules from the ChEMBL database. The new model obtained by this generative model has been evaluated based on the quantitative structure–activity relationship (QSAR). QSAR predicts the complex molecule and various parameters related to this molecule like log P and log D within a lesser period. However, this model has many limitations. A new technology that is known as deep learning has been introduced for the evaluations of drug molecules. This technique is more efficient than QSAR. Artificial intelligence-based tools like decision trees and support vector machines have been applied to the QSAR to overcome its limitations. Artificial intelligence-based tools like deep neural networks, algorithms, extreme learning machines etc., can be used in the virtual screening of a drug, and they can also be helpful in the prediction of activity and toxicity of a drug. The physicochemical properties (degree of ionization, partition coefficient, solubility etc.) can causes harmful effects on the pharmacokinetics properties. Thus, the various artificial intelligence models containing a large data set are used to predict the physicochemical properties [34]. Artificial intelligence-based algorithms can generate a drug designed with desirable properties. For the structure-based drug discovery, the 3D structure of the protein is more important. So, with the help of AI-based tools, this process is straightforward and accurate [35]. The algorithm that is used in the drug designing must contain SMILE strings, molecular descriptors, potential energy measurement, and the electron density around a molecule. The deep learning-based algorithm is used to design a graph to predict the solubility of a molecule. The artificial intelligence neu-

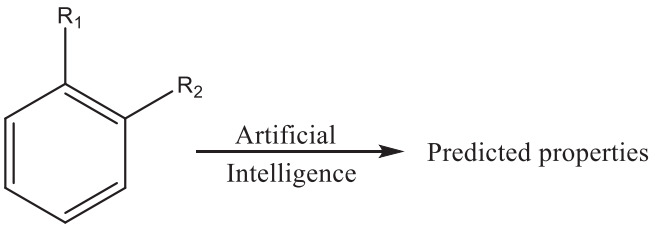

Fig. 5. Molecular property prediction by Artificial Intelligence [20].

Table 1
Summary of the role of artificial intelligence in chemistry.

S. NO.	Authors	Title	AI in chemistry	Application
1.	Retrosynthesis accessibility score (RAscore)- rapid machine-learned synthesizability classification from AI-driven retrosynthetic planning	A. Thakkar, V. Chadimova, E. J. Bjerrum, O. Engkvist, J. L. reymond	Artificial intelligence in retrosynthesis	- Aizynthfinder tool is used in retrosynthesis planning. - aximum of two hundred iterations and about fifty actions were determined by AI within lesser time [38].
2.	Chemistry in times of artificial intelligence	J. Gasteiger	Artificial intelligence in the prediction of reaction outcomes	- Quantum- based approach used in the determination of reaction outcomes. - CASREACT and REAXYS containing millions of data set used in the prediction of reaction outcomes [39].
3.	Computer-assisted design of complex organic syntheses	E. J. Corey, W. T. Wipke	Artificial intelligence in molecular designing	- AI helps to provide an alternate route for molecular design - Prioritize the compound which we want to synthesize. - De novo drug design based on artificial intelligence can generate a new molecule that contains desirable properties [40].
4.	Applications of neural networks to water and wastewater treatment plant operation	Z. Boger	Artificial intelligence in waste-water treatment	- Neural networks learn from the previously available data set. - The growing activity of neural networks used in the waste-water treatment [41].
5.	Nanoscale materials modeling using neural networks	Asproulis, Nikolas, Drikais, Dimitris	Artificial intelligence in nanotechnology	- AI is used in the determination of the structural properties of Nano-material. - AI-based algorithms can be trained by the available data set [42].
6.	Artificial intelligence in drug discovery	M. A. Sellwood, M. Ahmed, M. H. Segler, N. Brown	Artificial intelligence in drug discovery	- AI-based algorithms can synthesized and test the compound automatically and provide feedback for further decision making [43].
7.	Multi-task neural networks QSAR predictions	G. E. Dahl, N. Jaitly, R. Salakhutdinov	Artificial intelligence in molecular property prediction	- Alhelps in molecular property prediction. - AI can not only predict one endpoint, but it can predict multiple endpoints simultaneously [44].

ral network is further used in the prediction of dissociation constant [36].

2.7. Artificial intelligence in molecular property prediction

Once the molecule has been synthesized, then we need to know whether the synthesized molecule possesses all the properties of a molecule that we want to synthesize or not. Manually this process is arduous and time-consuming. Nevertheless, with the help of artificial intelligence, this process is easy and less time-consuming. The artificial intelligence-based algorithms have been applied to the molecule to predict its property like solubility, temperature, melting point, and other properties [37]. A machine-based model known as the BOB contains a large amount of data set that is useful in predicting the molecular properties such as polarizability, HOMO (highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital) of the molecule [3].

AI-based algoritms are particularly well suited to problems for which the physical laws that determine the molecular properties to be predicted are not exactly known, or when empirical relationships would be too complicated to establish. Moreover, AI can be used in combination with other prediction methods such as physical equations or empirical relationships, in order to obtain predictions which are even more accurate (Fig. 5).

Here, Table 1 contains the summary of recent literature work based on the role of artificial intelligence in the field of chemistry.

Since, Artificial Intelligence is still being developed and the relationship between chemistry and AI has a long way to go, the bond's future prospects appear to be bright. Artificial intelligence's future scope is projected to increase the area of chemical sciences by a factor of ten, as more ailments emerge and artificial intelligence in the field of chemistry radically assists scientists in producing potential technological breakthroughs in the field of science.

Such innovative strategies are expected to continue in the future, but it is necessary to ensure that the scientific community is well-informed on Artificial Intelligence's technological advancements. This combination will not only let scientists collect huge amounts of data and build algorithms for better use in the next decades, but it will also enable breakthroughs in a variety of fields with far-reaching implications for humanity.

3. Conclusion

To summarise, AI-discovered compounds are a fascinating topic to learn about. However, it is not implausible to see chemical sciences and Artificial Intelligence working together to better discoveries and data. This article is addressed to several chemists who are interested in the potential of AI in chemistry and also to the fresh researchers who are new to this area. With this review article one can check the progress made so far in this domain, by highlighting the past efforts that contain valuable lessons for the future. They can identify these lessons as a springboard, identify prospective current and future AI applications in chemistry. Since, artificial intelligence (AI) will play an increasingly dominant role in chemistry research and education, it's necessary to remember and record key early accomplishments. So far, the combination of AI and chemistry has led to the development of noteworthy technologies that have only served to benefit the scientific community.

CRediT authorship contribution statement

Neeru Choudhary: Data curation, Writing – original draft. **Ruchi Bharti:** Conceptualization, Supervision, Writing – review & editing, Project administration. **Renu Sharma:** Formal analysis, Validation, Supervision.

Declaration of Competing Interest

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

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