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REVIEW

Artificial Intelligence in Green Organic Chemistry: Pathway to Sustainable and Eco-Friendly Chemistry

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Artificial intelligence (AI) is playing an increasingly critical role in advancing green organic chemistry by optimizing chemical processes to minimize environmental impact. From predicting reaction outcomes to designing eco-friendly synthetic pathways, AI tools are contributing to sustainable chemical research. This review explores the application of AI in areas such as reaction optimization, solvent selection and waste reduction, all key aspects of green chemistry. Moreover, AI-driven approaches allow for the development of catalysts and reagents that reduce harmful byproducts and energy consumption. Despite these advancements, challenges remain in terms of data availability, integration with experimental workflows and ensuring the interpretability of AI models for chemists. This review also highlights the potential of AI to accelerate green chemistry innovation while maintaining alignment with the 12 principles of green chemistry. By addressing these challenges, AI can further enhance the sustainability of organic synthesis, paving the way for a greener chemical industry.

Keywords: Artificial intelligence, Green chemistry, Organic synthesis, Sustainability, Reaction optimization, Machine learning.

INTRODUCTION

Green organic chemistry seeks to mitigate the environmental and health impacts of chemical processes by adhering to the twelve principles of green chemistry, which emphasize minimizing waste, reducing toxicity and conserving energy [1,2]. In response to growing concerns about environmental degradation and resource depletion, green chemistry has become a critical focus in scientific research. This field aims to design chemical products and processes that are more sustainable, emphasizing the use of renewable feedstocks, safer solvents and energy-efficient methods [3].

Several key breakthrough in green organic chemistry have significantly advanced sustainable methodologies. These include the use of biocatalysis [4], where natural enzymes replace hazardous chemical catalysts, offering selective and eco-friendly transformations under mild conditions. The adoption of supercritical carbon dioxide ($scCO_2$) as a green solvent [5] provides an environmentally benign alternative to traditional solvents, while photoredox catalysis [6] leverages visible light to drive chemical reactions, reducing energy consumption. Moreover, innovations such as microwave-assisted organic synthesis (MAOS) and flow chemistry [7] enable faster, energy-efficient reactions with less waste. The development of solvent-free

and catalysis-free reactions [8] further exemplifies the move toward greener processes and the use of renewable feedstocks [9] from biomass helps reduce reliance on non-renewable resources. These breakthroughs underscore the shift toward more sustainable practices in chemistry.

Recent advancements in technology, particularly AI and machine learning (ML), are revolutionizing green organic chemistry by offering novel solutions to enhance sustainability. AI methods are increasingly applied to optimize chemical reactions, design eco-friendly processes and discover sustainable materials [10]. AI algorithms can analyze extensive experimental data to predict reaction outcomes, recommend greener solvents and catalysts and devise more efficient synthetic routes. This automation significantly reduces the time and resources needed for chemical discovery, making sustainable practices more attainable [11].

The significance of AI goes beyond optimization; it introduces innovative approaches to longstanding challenges. For instance, AI can swiftly screen numerous reaction conditions to identify those that minimize waste, predict environmentally friendly catalysts that reduce energy consumption and suggest renewable feedstock alternatives. AI-driven retrosynthesis can also propose multiple synthetic pathways, ranking them based on their environmental impact [12].

However, integrating AI into green chemistry presents challenges. High-quality, curated chemical datasets are often limited, impacting the accuracy of AI models [13]. Furthermore, many AI models function as "black boxes," lacking transparency in their prediction processes, which can hinder their acceptance among researchers [14]. Effective integration of AI into experimental workflows necessitates interdisciplinary collaboration among chemists, data scientists and AI specialists to ensure that AI tools are practical and interpretable [15].

This review explores the transformative role of AI in green organic chemistry, focusing on its applications in reaction optimization, solvent selection, waste reduction and catalyst design. It also addresses challenges related to data availability, model interpretability and interdisciplinary collaboration, providing a comprehensive overview of AI's contributions to advancing sustainable chemical processes.

AI in reaction optimization and predictive modeling

Machine learning (ML) in organic reaction prediction: The optimizing reaction conditions in organic chemistry is often a time-consuming process, involving the manipulation of temperatures, catalysts and solvents to achieve the highest yield with minimal resource use. Traditionally, this involves the laborious trial-and-error experimentation. However, ML offers a more efficient solution by analyzing vast datasets of historical reactions to identify patterns that lead to optimal outcomes. For example, ML models trained on reaction data can accurately predict key variables such as yield, reaction time and selectivity [16], allowing chemists to directly target the best conditions. This significantly reduces resource consumption and environmental impact.

A notable example is the work of Makarov *et al.* [17], who developed a random forest-based ML model to predict the yields of pyrrole and dipyrromethane condensation reactions with aldehydes. Trained on over 1,200 reactions, their model was integrated into a user-friendly web application, ChemPredictor (http://chem-predictor.isc-ras.ru/reaction/yield/), where users can input reaction components and temperature to predict yields.

The application of AI models such as neural networks and random forests is particularly valuable for modeling complex reaction dynamics, especially when non-linear relationships between variables are involved–common in organic reactions [18]. Beyond optimization, these models can also predict reaction outcomes in unexplored conditions, offering the possibility of discovering greener reaction pathways that reduce environmental harm.

Coley *et al.* [19] further demonstrated AI's potential in predicting reaction outcomes by combining traditional reaction templates with the pattern recognition capabilities of neural networks. Their model, trained on 15,000 experimental reactions from U.S. patents, ranked potential products by focusing on the transformation from reactants to products, rather than overall molecular structures. In 5-fold cross-validation, the model successfully ranked the major product as the top candidate in 71.8% of cases, within the top 3 in 86.7% and within the top 5 in 90.8%.

Fig. 1 illustrates the retrosynthetic analysis of pyrazoline derivatives, a class of heterocyclic compounds with significant pharmacological applications, as predicted by the AI-powered platform Syntelly. In this figure, the target molecule, a pyrazoline derivative, is shown in the center, with the AI suggesting a series of sequential disconnections that reduce the complexity of the molecule. Each step represents a synthetic transformation in reverse, providing insight into the starting materials required to synthesize the target compound. The analysis highlights key reaction intermediates, reagents and the conditions needed for each transformation [20]. However, none of the predicted routes was considered viable compared. This is primarily due to their ease of availability and the simpler methods required for their preparation, making them more suitable for efficient synthesis.

Syntelly's AI-powered system predicts these reaction pathways by analyzing extensive chemical databases and using ML algorithms to suggest efficient, eco-friendly routes [21]. This approach aligns with green chemistry principles by proposing synthetic methods that reduce waste, minimize the use of hazardous reagents and optimize energy efficiency.

AI is increasingly being leveraged to design reactions with a lower environmental impact. For instance, IBM RXN for chemistry [22], an AI-driven tool, predicts chemical reactions and their optimal conditions, helping chemists minimize resource use and enhance efficiency. Similarly, Chematica [23], an AI-powered retrosynthesis platform, identifies reaction pathways that reduce steps, waste and energy consumption, aligning with the principles of green chemistry.

Catalyst and reagent design: Catalysts are vital to green organic chemistry as they lower activation energy, enabling reactions to occur under milder, more energy-efficient conditions [24]. AI has significantly enhanced catalyst design by predicting performance across a wide range of reactions, identi-

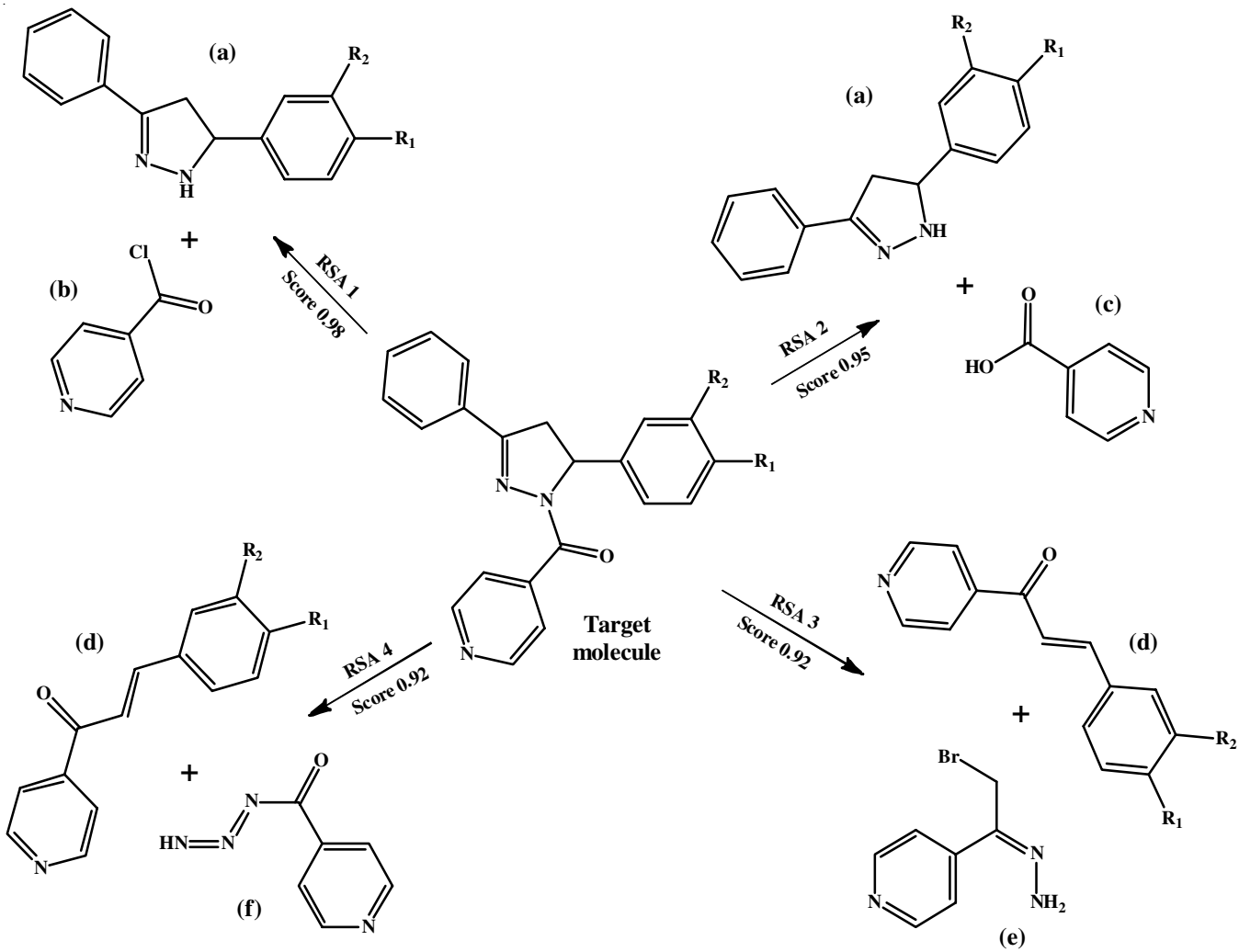

Fig. 1. The retrosynthetic analysis of pyrazoline derivatives predicted by Syntelly [Ref. 21]

fying catalysts that minimize waste, reduce toxicity and lower energy consumption [25].

One prominent example is Park *et al.* [26] introduced the Chemical Markdown Language (CMDL), a domain-specific language that enables seamless integration of historical experimental data to fine-tune regression transformer (RT) models for molecular design. This method has been applied to generate and experimentally validate catalysts and polymers for ring-opening polymerization, with broader applications to other polymer classes. The CMDL-tuned models preserved key functional groups, ensuring successful experimental outcomes and showcasing its versatility in translating historical data into actionable predictive models.

Mazheika *et al.* [27] demonstrated how AI-based subgroup discovery can guide the rational design of catalytic materials. Their model, trained on first-principles data, identified catalyst "genes" that control CO_2 activation for chemical conversion. By correlating specific gene combinations with efficient C-O bond elongation and reduced OCO-angle, they proposed promising new catalysts for CO_2 conversion. This emphasizes the potential of AI to reveal the mechanistic details and enhance the development of more efficient catalysts.

AI is also making significant strides in replacing toxic reagents with biodegradable alternatives [28]. ML models have been instrumental in discovering organocatalysts–organic molecules that act as sustainable catalysts, typically less harmful than traditional metal-based options [29]. Furthermore, AI is playing an increasingly critical role in enzyme design, offering highly specific and sustainable biocatalysts, which provide efficient and eco-friendly reaction pathways [30]. For example, Gallarati *et al.* [31] applied an inverse design strategy using the open-source genetic algorithm NaviCatGA and the OSCAR database of organocatalysts. Focusing on the Pictet–Spengler condensation reaction, they curated a database of 820 reactions to train models of selectivity and activity. Through evolutionary experiments across millions of possible catalysts, they identified privileged catalysts and extracted structure–performance relationships. This demonstrates AI's ability to streamline complex chemical space exploration and optimize catalyst design. Similarly, Zhou & Huang [32] reviewed the structure-based and ML guided enzyme design, emphasizing the integration of traditional molecular simulations with AI techniques. They highlighted the importance of building comprehensive databases and advanced algorithms to develop predictive models

for enzyme design. These models are essential for exploring sequence fitness landscapes and creating effective biocatalysts.

Table-1 provides an overview of several AI-powered tools and platforms that are significantly advancing research in green organic chemistry. These tools utilize AI to optimize various aspects of chemical synthesis, such as reaction prediction, retrosynthesis, catalyst design, solvent selection and waste reduction, thereby aligning with the 12 principles of green chemistry.

Overall, AI-driven innovations in catalyst and enzyme design are transforming green chemistry. By uncovering new catalysts, optimizing reaction conditions and replacing harmful reagents with sustainable alternatives, AI is contributing to the development of more environmentally friendly chemical processes. Each example highlights the interrelation of AI, sustainability and chemistry, demonstrating their convergence in tackling contemporary environmental issues.

AI-Driven solvent selection and waste reduction

Solvent selection: Solvents play a significant role in the environmental impact of chemical reactions. Many traditional solvents, such as benzene and dichloromethane, are toxic, non-biodegradable and difficult to dispose of safely. Green chemistry emphasizes the shift towards safer, more sustainable alternatives. AI has become a valuable tool in this pursuit by analyzing solvent properties and predicting their behaviour under specific reaction conditions. ML algorithms can recommend non-toxic, biodegradable and recyclable solvents, aligning with the principles of green chemistry [33,34].

A significant contribution to this effort by Sels *et al.* [35] developed an AI-driven approach for solvent selection and substitution. They used a neural network, specifically the Kohonen Self-organizing map, to cluster a solvent database based on the physical properties. These clusters were then validated chemically and statistically and visualized in a user-friendly interface *via* the SUSSOL (Sustainable Solvents Selection and Substitution Software) tool. SUSSOL allows users to explore solvent options and generate ranked alternatives for specific solvents based on safety, health and environmental criteria. A dependable platform for picking greener, more sustainable solvents, the tool was proven useful in case studies, which typically matched with recommendations from existing literature.

AI has also been used to identify greener solvent alternatives, such as ionic liquids and supercritical fluids, which offer lower toxicity and volatility while maintaining high efficiency in various organic reactions. ML models can evaluate and compare the environmental footprints of different solvents based on factors like toxicity, biodegradability and energy efficiency, guiding chemists in making sustainable choices [36]. Lemaoui *et al.* [37] further advanced the use of AI in solvent design by combining molecular modeling with ensemble deep learning to predict multiple properties of ionic liquids (ILs). Their study, based on a dataset of 73,847 data points from 2,917 ILs, tested eight ML models, finding that artificial neural networks (ANNs) offered the most accurate predictions. The ANN model achieved high R^2 values across several properties, including 0.993 for density and 0.907 for viscosity. Furthermore, their comprehensive screening of 303,880 ILs led to the development of an "Inverse Designer Tool" for selecting ILs based on specific green chemistry criteria, aiding in the eco-efficient design of solvents for industrial applications.

The role of AI in promoting safer and more sustainable chemical processes continues to expand. Several companies have developed bespoke solvent selection guides to assist scientists in making environmentally conscious choices. For example, the Solvent Selection Guides from GSK [38], Pfizer [39] and Sanofi [40] use AI to help chemists identify solvents that align with environmental and safety standards. In addition, AI-driven research has recommended the use of supercritical CO_2 (SC-CO_2) as a greener solvent, significantly reducing the ecological impact of chemical reactions. Based on these advan-

TABLE-1
DETAILS OF SOME AI-POWERED TOOLS AND PLATFORMS IN GREEN CHEMISTRY RESEARCH

Tool/Platform	Functionality	Example of application
Open reaction database (ORD)	Provides open-access data for AI model training in green chemistry	ORD was used by chemists and data scientists to develop AI models for predicting sustainable synthesis pathways for drug discovery
Toxicity estimation software tool (T.E.S.T.)	Uses AI to predict chemical toxicity for green chemistry applications	T.E.S.T. predicted the toxicity of by-products in a pharmaceutical synthesis, allowing chemists to replace harmful reagents early in the process
IBM RXN for chemistry	AI-powered retrosynthesis and reaction prediction platform	IBM RXN predicted greener synthetic pathways for organic compounds, resulting in a 30% reduction in hazardous waste generation in laboratory trials
ASKCOS	AI-based tool for retrosynthetic analysis, offering multiple synthetic pathways for a given target molecule	ASKCOS proposed a sustainable synthetic route for a pharmaceutical intermediate, minimizing solvent waste by 25%
Chemputer	A programmable, automated chemistry platform that uses AI to execute chemical reactions	The Chemputer automated an AI-predicted green synthesis pathway for a bioactive molecule, reducing energy consumption by 40%
DeepChem	A ML library designed for chemistry and materials science	DeepChem was used to develop AI models that predicted eco-friendly catalysts for CO_2 capture
Reaction mechanism generator (RMG)	Open-source AI tool for generating detailed reaction mechanisms and kinetics	RMG generated a sustainable catalytic pathway for biomass conversion to biofuels, minimizing by-products and energy input
Chematica (now Synthia)	AI-based retrosynthesis tool that predicts synthetic routes with a focus on sustainability and cost-effectiveness	Chematica suggested a green synthetic route for a complex pharmaceutical, reducing hazardous reagent use by 20%

cements, Huwaimel & Alobaida [41] used ML to explore the solubility of tamoxifen in SC-CO_2. By applying Adaboost methods, they optimized three models *viz*. K-nearest Neighbor (KNN), Theil-Sen Regression (TSR) and Gaussian Process Regression (GPR) with pressure and temperature as input variables. Their models demonstrated strong predictive performance, with ADA-KNN achieving an R^2 of 0.996, the highest among the models. This approach highlights the potential of AI in advancing green chemistry, offering precise solubility predictions and facilitating the design of environmentally friendly solvents. This interconnected use of AI in solvent selection and optimization underscores its critical role in advancing sustainable chemistry practices.

Minimizing byproducts and waste: Waste reduction is a cornerstone of green chemistry. Traditional synthetic routes often involve multiple steps, each generating its own waste [42]. AI enhances these pathways by analyzing reaction data to suggest more efficient routes that minimize byproducts and reduce the number of steps required. By identifying alternative pathways or conditions that avoid unwanted byproducts, AI significantly lowers the environmental footprint of organic synthesis [43].

Liu & Hein [44] examine the revolutionary effect of automation, analytics and artificial intelligence on chemical synthesis. Their work highlights the transformative impact of these technologies in enabling real-time reaction monitoring, data-driven decision-making and autonomous experimentation. With AI tools, chemists can analyze extensive datasets to optimize reaction conditions more efficiently, which reduces errors and waste, thereby supporting the development of scalable and sustainable synthetic pathways.

Thus, Kariofillis *et al.* [45] demonstrated the integration of data science techniques to guide substrate scope analysis in a Ni/photoredox-catalyzed cross-coupling reaction using acetals as radical sources. They employed tools such as DFT featurization, dimensionality reduction and hierarchical clustering to develop a diverse collection of aryl bromides. By mapping these methods onto the substrate space, they identified areas of sparse coverage and trends in reaction yields, which highlighted regions of high efficiency and potential functional group incompatibilities. This approach underscores how data science can enhance reaction optimization and waste reduction.

In a different application, Jorayev *et al.* [46] optimized a chemical route starting from biowaste derived mixtures, focusing on converting waste terpenes to *p*-cymene. Without a detailed kinetic model, they utilized the Bayesian optimization algorithm TS-EMO (two-stage evolutionary multi-objective optimization) to enhance the first two reaction steps for maximum conversion and selectivity. This successful application of TS-EMO highlights its effectiveness in reaction optimization even without prior kinetic data.

Furthermore, AI-based retrosynthesis tools play a crucial role in designing pathways that minimize hazardous byproducts. For instance, the Synthia platform generates greener synthetic routes by avoiding toxic byproducts and AI is also utilized in flow chemistry to optimize continuous reactions in real-time [47,48].

A case study by Hardy *et al.* [49] exemplifies the application of computer-assisted synthesis planning (CASP) through its focus on pupukeanane natural products. Using the Synthia™ program, they generated and compared synthetic pathways, validating existing methods and proposing novel synthesis strategies for unprepared congeners. This study highlights the strategic value of CASP in designing efficient routes for complex molecules.

Additionally, in their assessment of AI applications in retro-biosynthesis, Gricourt *et al*. [50] explore into the ways in which AI-driven tools streamline the process of designing synthetic pathways. The review covers template based methods and generative models, emphasizing AI's role in minimizing hazardous byproducts and aligning with green chemistry principles. It also outlines advancements, challenges and future directions in AI-powered retrosynthesis.

Finally, Ishida *et al.* [51] introduced "ReTReK", a CASP application integrating ML with retrosynthesis knowledge to enhance synthetic route design. Their experimental results showed that ReTReK effectively identifies preferred synthetic routes by leveraging integrated knowledge, outperforming methods without such data. This development illustrates AI's potential to improve CASP applications and contribute to more efficient, greener synthetic strategies.

Enhancing sustainability with AI in catalysis

Catalysis optimization: Catalysis plays a crucial role in advancing green organic chemistry and AI is making significant contributions in this area. By designing more efficient catalysts, AI helps reduce the energy required for chemical reactions and minimizes harmful byproducts. One of the AI's primary functions is predicting the performance of various catalytic systems, enabling researchers to identify catalysts that are both effective and environmental friendly [52,53].

Kalikadien *et al.* [54] conducted an indepth study on the enantioselective hydrogenation of olefins using Rh-based chiral catalysts, a process explored for over 50 years. Although selecting the right catalyst for desired reactivity or selectivity might seem straightforward, the process of ligand engineering for new prochiral olefins often relies on empirical trial and error. The study aimed to determine if ML techniques could streamline the identification of efficient chiral ligands.

The researchers created a large dataset of Rh-catalyzed asymmetric olefin hydrogenation results specifically designed for ML applications. They developed a computational framework for automated quantum chemistry based featurization of catalyst structures, incorporating both computationally intensive and less demanding descriptors into their ML pipeline. This approach was used to predict selectivity and reactivity. While out-of-domain predictions showed limited success, even with the most advanced descriptors, in-domain applications achieved moderate success, particularly in predicting conversion. This underscores the importance of balancing the cost and benefit of computational descriptors and the need for tailored designs. The study also highlights persistent challenges in predicting enantioselectivity, especially with small datasets, emphasizing the need for diverse datasets and mechanistic insights to enhance the reliability of statistical models.

AI-based methods, such as genetic algorithms and neural networks, further advance catalysis by analyzing extensive catalytic data to predict the performance of new or existing catalysts under various conditions. These methods have led to the discovery of more efficient catalysts that align with green chemistry principles by reducing the use of toxic metals and harsh reaction conditions. Moreover, AI helps optimize catalyst loading, which reduces material waste [55].

Suvarna & Ramírez [56] also emphasized the importance of accelerating catalyst discovery to address global challenges in energy, sustainability and healthcare. Over the past decade, data science concepts have increasingly been applied to catalysis research. The authors categorize studies into deductive or inductive approaches and analyze various catalytic tasks, model reactions, data representations and algorithm choices.

Their review identifies key advancements and opportunities for cross-disciplinary knowledge transfer but also notes a significant gap in integrating data science with experimental catalysis. To address this, they propose a framework based on four pillars of data science–descriptive, predictive, causal and prescriptive analytics. They advocate for incorporating these analytics into experimental workflows and standardizing data to drive future research in digital catalysis, promoting a more systematic and efficient approach to catalyst development.

AI optimization in catalysis is also exemplified by the development of photo- and electrocatalysts that use less energy and minimize toxic byproducts. For instance, AI models have been used to design photocatalysts that harness sunlight for reactions such as CO_2 reduction to fuels, aligning with sustainability goals. Moreover, AI has been employed to predict catalyst performance in hydrogenation reactions, leading to the discovery of catalysts that operate under milder conditions and reduce energy consumption [57].

In a related study, Li *et al.* [58] explored the catalytic potential of conjugated organic photoredox catalysts (OPCs), which promote a wide range of chemical transformations. Predicting the catalytic activities of OPCs is challenging due to the complex interplay of various properties, making traditional design and trial-and-error methods less effective. To address this challenge, the authors introduced a two-step data-driven approach for targeted OPC synthesis and reaction optimization in metallophotocatalysis. Using Bayesian optimization and molecular descriptors, they identified promising OPC candidates from a virtual library of 560 molecules. This method enabled the discovery of OPC formulations that rivaled iridium catalysts, despite testing only a small fraction (2.4%) of the possible reaction conditions.

Renewable feedstocks: AI is significantly transforming the use of renewable feedstocks, offering advancements over traditional petroleum-based sources [59]. By analyzing extensive datasets of chemical reactions, AI can identify alternative, renewable feedstocks from biomass and other sustainable sources. This capability supports the development of green synthetic pathways, reducing reliance on fossil fuels and minimizing the carbon footprint of chemical production [60,61]. Osman *et al*. [62] investigated the optimization of biodiesel production from waste materials through computational chemistry and machine learning. Their research highlights the role of these technologies in various aspects of biodiesel production, including catalyst design, reaction optimization and waste feedstock analysis. They identify waste feedstocks such as used cooking oil, animal fat, vegetable oil, algae, fish waste, municipal solid waste and sewage sludge as key sources for biodiesel. Significantly, waste cooking oil alone contributes to about 10% of global biodiesel production, with restaurants generating over 1,000,000 m^3 annually. Microalgae, with its high oil yield, is particularly efficient, producing up to 31 times more oil than palm oil. Enhancing biodiesel production and promoting the sustainable use of waste feedstocks can be achieved through computational and ML approaches, as demonstrated in this work.

Zhao *et al.* [63] applied ML to optimize the oxidative pyrolysis of biomass in a fixed-bed reactor. They developed an ANN model to predict yields of various products including water, tar, gas, char and CO/CO_2 concentrations. The study revealed that oxidative pyrolysis is more complex than inert pyrolysis due to the influence of oxygen on both homogeneous and heterogeneous oxidation processes. By using a combination of logsig and purelin transfer functions in the ANN and optimizing the model with particle swarm optimization (PSO), they achieved a relative error below 10%. This demonstrates the potential of ML to improve biomass conversion processes and enhance the use of renewable feedstocks for bioenergy production.

Additionally, AI models are increasingly used to identify bio-based alternatives for traditional petroleum-derived reagents in organic synthesis. These models help predict the performance of renewable feedstocks in various chemical reactions, facilitating the design of greener production processes [64]. Jana *et al.* [65] focused on optimizing biodiesel production from waste cooking oil using a CaO-based catalyst derived from solid ostrich eggshells. They compared several ML techniques, including Type 1 Fuzzy logic system (T1FLS), response surface methodology (RSM), adaptive neuro-fuzzy inference system (ANFIS) and Type 2 fuzzy logic system (T2FLS). The T2FLS model demonstrated the highest accuracy with a determination coefficient (R^2) of 99.1%, exhibiting its superior capability in handling dynamic chemical processes.

Sultana *et al*. [66] examined the effects of light-dark cycles and NaNO dosage on the development and lipid production of Chlorella kessleri, a microalgal biomass with considerable bioenergy potential. They developed response surface methodology (RSM) and support vector regression (SVR) models, with Bayesian optimization (BOA) improving SVR accuracy. Combining BOA with the crow search algorithm, they identified optimal conditions for maximizing specific growth rate (SGR), biomass productivity and lipid productivity. This demonstrates the effectiveness of integrating ML and optimization techniques to enhance microalgal biomass productivity for bioenergy applications.

Moreover, ML has been applied to optimize the conversion of lignocellulosic biomass into valuable chemicals and identify sustainable, bio-based solvents, such as lactic acid and ethyl lactate, which are more environmental friendly than traditional

solvents [67]. Sonwai *et al.* [68] utilized ML to predict specific methane yields (SMY) from lignocellulosic biomass (LB) using a dataset with 14 features. The random forest model was the most effective, achieving a coefficient of determination (R^2) of 0.85 and a root mean square error of 0.06. They discovered that cellulose content had the greatest impact on SMY and identified an optimal LB-to-manure ratio of 1:1 for biogas production. This study highlights the successful application of ML in modeling and optimizing anaerobic digestion processes, thus enhancing biogas production efficiency.

Integration of AI with experimental workflows:

Data availability and quality: A significant challenge in applying AI to green organic chemistry is the limited availability and quality of data. ML models rely on large datasets to accurately predict reaction outcomes, solvent behaviour and catalyst efficiency [69]. However, high-quality experimental data is often scarce or restricted, which limits the development of dependable AI models. Furthermore, conventional chemistry data may not be directly applicable to green chemistry, where sustainable and innovative approaches are emphasized, complicating the training of AI systems [70,71].

To overcome these barriers, there is a growing push toward open-access databases and data-sharing initiatives within the chemical sciences [72,73]. For instance, the Materials Project [74] and the open reaction database [75] offer freely accessible reaction data that can be utilized to train AI models. These collaborative efforts are essential for improving the accuracy and effectiveness of AI-driven tools in advancing green organic chemistry.

Interdisciplinary collaboration: To unlock the full potential of AI in green organic chemistry, collaboration between chemists, data scientists and AI experts is essential. Chemists bring critical domain knowledge to interpret AI-generated predictions, while data scientists focus on building robust models capable of generalizing to new datasets [76,77]. This interdisciplinary approach is key to effectively integrating AI into experimental workflows. A vital aspect of collaboration is enhancing the interpretability of AI models. For chemists to rely on and employ AI predictions, they require understanding of the mechanisms by which the models produce their suggestions. Recent advancements in explainable AI (XAI) are addressing this by making AI models more transparent and interpretable, fostering trust and enabling broader adoption in the laboratory [78].

The success of AI in green chemistry hinges on multidisciplinary efforts. For example, *in silico* medicine's pharma. AI project–a commercially available, end-to-end generative AI software and robotics platform–enhances pharmaceutical research productivity by combining expertise from chemists, AI specialists and data scientists [79]. Explainable AI methods, such as SHAP (SHapley Additive Explanations), further contribute by making AI models more transparent to chemists, bridging the gap between AI predictions and practical applications [80].

Role of AI in 12 principles of green chemistry: AI is increasingly pivotal in advancing sustainability in organic chemistry by aligning with the 12 principles of green chemistry, which aim to reduce environmental and health impacts. Each concept is supported by AI in the following ways:

Prevention: AI-powered retrosynthesis tools, such as ASKCOS, optimize synthetic pathways to minimize waste by suggesting routes that generate fewer byproducts [81].

Atom economy: AI tools like Chemprop enhance atom economy by proposing synthetic routes that maximize the incorporation of starting materials into the final product, thus reducing waste [82].

Less hazardous chemical syntheses: AI models identify safer alternatives to hazardous reagents, such as predicting non-toxic substitutes for cyanide-based reactions [83].

Designing safer chemicals: ML platforms, like syntelly, predict chemical toxicity and assist in designing safer compounds by evaluating organ toxicity, environmental impact and bioaccumulation [84].

Safer solvents and auxiliaries: AI tools, such as ILThermo Database, help select safer, eco-friendly solvents by analyzing extensive solvent property data and suggesting alternatives to hazardous solvents [85].

Design for energy efficiency: AI-driven optimization tools in microwave-assisted organic synthesis (MAOS) reduce energy consumption by predicting optimal reaction conditions [86].

Use of renewable feedstocks: AI advances biofuel technologies by optimizing production processes, screening new materials and assessing economic and environmental impacts, thus reducing reliance on fossil fuels [87].

Reduce derivatives: AI-based retrosynthesis tools, like the Molecular Transformer model, streamline processes by eliminating unnecessary derivatization steps, reducing reagent use and waste [88].

Catalysis: AI enhances the design of efficient organocatalysts and biocatalysts, predicting catalyst behaviour and optimizing enzyme design for greener and more sustainable chemical processes [89].

Design for degradation: Artificial intelligence models forecast biodegradability, facilitating the development of compounds that breakdown into non-toxic byproducts. The online chemical modeling environment (OCHEM) provides tools for accurate biodegradability prediction and structural feature analysis [90].

Real-time analysis for pollution prevention: AI-based systems monitor reactions in real time, predicting hazardous byproducts and allowing adjustments to prevent pollution. For example, AI models have optimized phenol removal from wastewater using a Photo-Fenton reagent [91].

Inherently safer chemistry for accident prevention: AI predicts hazardous reaction conditions and suggests safer alternatives. An explainable AI model with convolutional neural networks achieves a low false negative rate, enhancing safety by identifying critical substructures and addressing data imbalance [92].

The 12 principles of green chemistry initially proposed by Anastas & Warner [93] provide a framework for designing the chemical processes and products which are environmental friendly and sustainable. These principles aim to minimize the negative environmental and health impacts of chemical

production by reducing waste, conserving energy and avoiding the use of hazardous substances.

AI's impact on reducing energy use, enhancing safety and minimizing waste is particularly significant. AI facilitates sustainable chemical processes by optimizing reaction conditions, identifying safer ingredients and minimizing waste. As AI technologies advance, their role in green chemistry will continue to grow, fostering more eco-friendly and efficient chemical processes.

Challenges and opportunities

Challenges

Data quality and availability: High-quality datasets are essential for training AI models effectively, but comprehensive datasets in the context of green organic chemistry are often limited. This limitation is critical as insufficient or poorly curated data can lead to biased, unreliable or inaccurate predictions, undermining the effectiveness of AI tools in advancing sustainable chemistry. For example, green chemistry often focuses on eco-friendly solvent selection, but the available datasets related to these solvents may lack the diversity and completeness needed for robust AI training. Additionally, in emerging areas of green chemistry, there might not be enough historical data to adequately train models, further complicating AI's role in this field. Expanding collaborative data-sharing initiatives and creating standardized datasets across industries could help overcome this challenge [94].

Complexity of chemical systems: Organic reactions typically involve complex, multi-step processes with numerous variables, including solvents, catalysts and reagents. AI models, particularly ML algorithms, may struggle to fully capture the intricate, non-linear relationships in these systems. This challenge becomes even more pronounced in green chemistry, where eco-friendly reactions must account for both sustainability and efficiency. For instance, ML models trained to optimize specific reactions, like the Suzuki-Miyaura coupling and Buchwald–Hartwig coupling reactions, may not be easily transferable to greener alternatives that use different, more sustainable reagents and conditions. Moreover, many green chemistry processes involve dynamic systems where reactions are influenced by real time conditions like temperature, pH and pressure, making prediction models even more complex to generalize effectively [95].

Interdisciplinary knowledge: Integrating AI into green chemistry necessitates collaboration between chemists, data scientists and environmental experts. These fields have distinct terminologies, methodologies and approaches, which can lead to communication gaps and hinder collaboration. Developing effective AI-driven solutions for green chemistry requires a deep understanding of both domains: chemists need to understand AI's capabilities and limitations, while AI researchers must grasp the nuances of chemical processes. A collaboration between IBM and the University of Toronto that developed a synthesis prediction tool demonstrates the value of such interdisciplinary efforts but also highlights the learning curve involved. To overcome these challenges, fostering interdisciplinary education and creating shared knowledge platforms can streamline collaboration and facilitate better AI integration into green chemical research [96-98].

Scalability and generalization: AI models developed for specific green chemistry reactions may not generalize well to other contexts or processes. For instance, an AI model trained to optimize a single reaction under specific conditions might perform poorly when applied to different reactions or eco-friendly synthesis routes. This lack of generalization is a significant hurdle in scaling AI applications across different chemical industries and processes. Ensuring scalability is essential for AI to have a broader impact on green chemistry, particularly in industries that require flexibility and adaptability in production. Emerging techniques such as transfer learning, where knowledge gained from one model is applied to another related problem, offer a promising approach for enhancing AI generalization in green chemistry. However, further research is needed to fine-tune these models so they can be reliably applied to new and diverse chemical systems [99].

Ethical and regulatory concerns: AI's use in chemistry raises ethical and regulatory issues, including data privacy, intellectual property and potential misuse. Establishing clear guidelines and regulations for AI in chemical research is necessary for responsible implementation. The use of AI in green chemistry needs to comply with ethical and regulatory guidelines to ensure sustainability and safety. Ethical considerations surrounding the environmental impact of AI itself, particularly in data centers and computing power, pose a challenge to its alignment with green chemistry's sustainability goals. Fig. 2 illustrates the key ethical considerations that arise during the integration of AI in the research and development process for quantum chemical simulations [100]. As AI becomes increasingly central to advancing computational chemistry, these considerations ensure that the technology is implemented responsibly, with a focus on transparency, safety and sustainability.

Energy consumption of AI models: Training large AI models requires substantial computational power, which directly translates into high energy consumption. This presents a paradox, as AI is often viewed as a tool to promote sustainability in green chemistry, yet its own carbon footprint can be quite large [101]. Strubell *et al.* [102] highlighted the environmental cost of training large AI models, revealing that a single model could emit as much CO_2 as five cars over their lifetime. This energy consumption poses a challenge to the sustainability goals of green chemistry. Efforts are being made to mitigate this issue, such as developing more energy-efficient algorithms and hardware, or incorporating renewable energy sources into AI infrastructure. Nonetheless, balancing the environmental costs of AI with its potential benefits for advancing green chemistry remains a critical challenge. Table-2 compares AI models based on their energy consumption (kWh) and environmental benefits, focusing on applications in green chemistry. Energy consumption is estimated based on model training and execution, while environmental benefits highlight the models' contributions to waste reduction, efficiency and sustainability.

Opportunities

Enhanced efficiency and sustainability optimization of synthesis pathways: AI can significantly enhance the efficiency and sustainability of chemical processes by optimizing

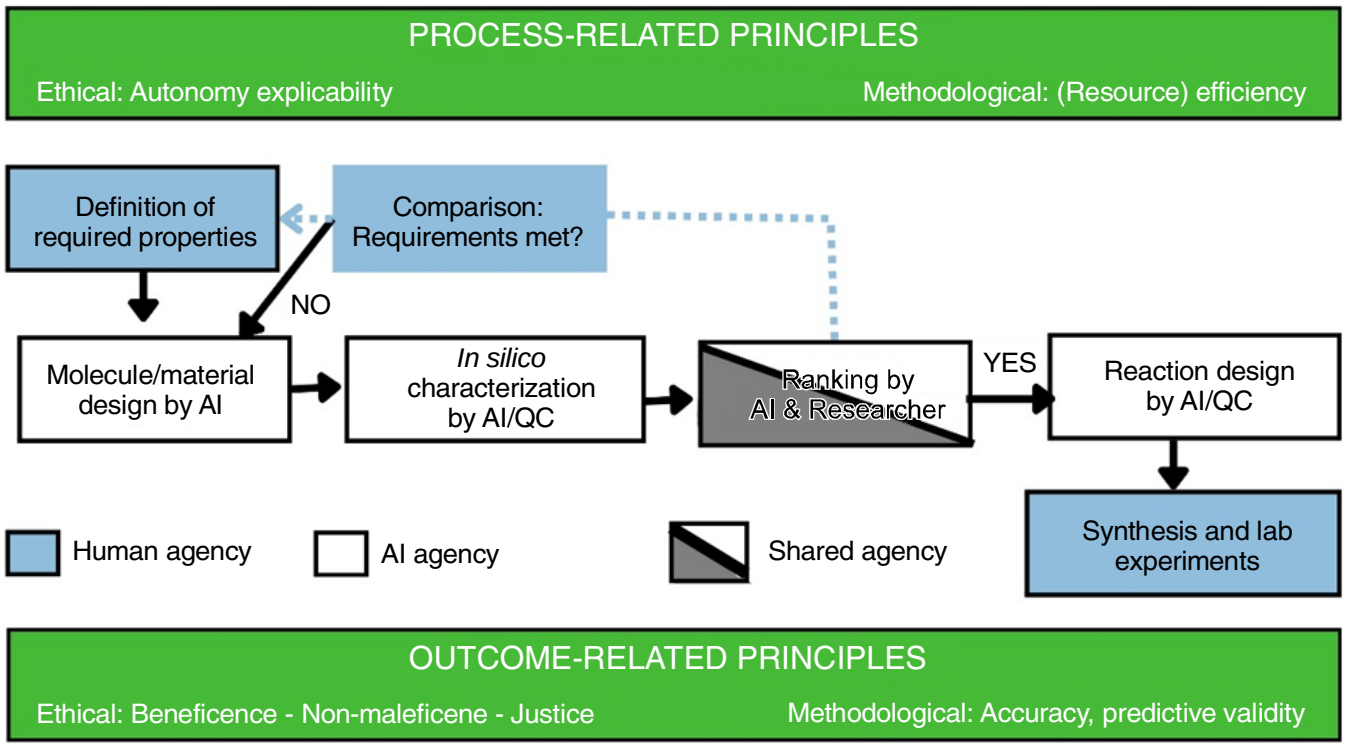

Fig. 2. Pathways for the ethical considerations in AI driven research and development process for quantum chemical simulations [Ref. 100]

TABLE-2
COMPARISON OF AI MODELS ENERGY CONSUMPTION AND ENVIRONMENTAL BENEFITS IN GREEN ORGANIC CHEMISTRY

AI model type	Energy consumption (kWh)	Environmental benefits
Deep neural networks (DNN)	High (~200 kWh for large models)	High accuracy in predicting reaction pathways, reducing trial-and-error experiments
Random forest (RF)	Medium (~50-70 kWh)	Effective in optimizing reaction conditions, solvent selection
Support vector machines (SVM)	Medium (~30-50 kWh)	Moderate accuracy but efficient in small datasets, reducing computational waste
Gaussian process regression (GPR)	Low (~10-20 kWh)	Highly interpretable, balances energy use and prediction efficiency
Genetic algorithms (GA)	Low (~10 kWh)	Adaptive optimization of processes, reduces chemical waste
Convolutional neural networks (CNN)	High (~150-180 kWh)	Excellent for pattern recognition in complex data, but energy-intensive
Reinforcement learning (RL)	High (~120-150 kWh)	Strong in decision-making tasks, reducing energy consumption in synthetic route optimization
k-Nearest neighbors (k-NN)	Low (~5-15 kWh)	Simple model, low energy usage, effective for quick predictions with smaller datasets
Bayesian networks (BN)	Medium (~40-60 kWh)	Efficient in uncertainty modeling, improves sustainability through probabilistic predictions

reaction conditions, predicting greener alternatives and reducing waste. This leads to more sustainable practices and reduced environmental impact. In traditional chemistry, the optimization of reaction conditions, such as temperature, pressure, solvent choice and catalyst selection, often requires time consuming experimentation. AI, particularly ML algorithms, can efficiently analyze large datasets and predict the optimal conditions for specific reactions, minimizing the use of hazardous materials, energy and time. For example, AI has been shown to optimize catalytic hydrogenation reactions, increasing yield while reducing waste and resource consumption, thereby contributing to greener synthetic routes. This not only supports the principles of green chemistry but also has direct implications for industrial applications where efficiency and sustainability are paramount [103].

Accelerating discovery and innovation enhanced catalyst design: AI accelerates the discovery of new materials, catalysts and reaction pathways by analyzing large datasets, offering insights that would be difficult to obtain through traditional trial-and-error methods. This capability speeds up the development of new pharmaceuticals, materials and chemicals, driving innovation in the field. An ability of AI to process vast amounts of data allows for faster identification of ecofriendly catalysts that are essential for sustainable chemical processes. For example, Wang & Jiang [104] and Lin *et al.* [105] used ML to predict the activity of metal-organic frameworks (MOFs), a class of materials known for their potential as green catalysts. By rapidly screening a variety of materials, AI enables the discovery of highly efficient and environmental friendly catalysts that can be used in industrial processes, reducing reliance on

toxic or rare materials. This accelerates the development of cleaner chemical technologies and supports a more sustainable chemical industry [104,105].

Personalized and adaptive approaches: AI enables personalized and adaptive approaches to green chemistry by tailoring reaction conditions to specific substrates, reactants and desired outcomes. In traditional chemistry, reaction conditions are often optimized for general scenarios, but AI allows for more precise customization of these conditions to maximize efficiency and sustainability for specific chemical processes. AI-driven systems can monitor and adjust reactions in real-time, making adaptive changes based on the conditions and inputs at any given moment. This leads to dynamic control of processes, optimizing energy usage, reducing waste and improving yields. For instance, real-time process monitoring using AI was successfully applied in green chemistry to reduce resource consumption, with the system making adaptive adjustments to reaction conditions. Such systems are particularly beneficial in industrial settings, where real-time adaptability can lead to significant reductions in material waste and energy consumption, aligning with the principles of green chemistry [106,107].

Improved safety and risk management-predictive toxicology: AI improves safety by predicting potential hazards and optimizing reaction conditions to minimize risks associated with chemical reactions and byproducts. Traditional methods for assessing the toxicity of chemicals and their environmental impact are often slow and costly. AI-driven predictive toxicology models enable the early identification of potentially hazardous substances, allowing chemists to avoid dangerous materials or design safer alternatives during the early stages of chemical development. The Toxicity Estimation Software Tool (T.E.S.T.), developed by the U.S. Environmental Protection Agency (EPA), leverages ML to predict the toxicity of chemicals and is widely used in green chemistry. By providing early warnings about toxic or harmful substances, AI tools like T.E.S.T. help to enhance overall safety and ensure that chemical processes align with the ethical and regulatory requirements of sustainable chemistry. This contributes to reducing occupational and environmental hazards in chemical manufacturing [108].

Advancement of green chemistry principles: AI supports the advancement of green chemistry by integrating sustainable principles into the design, optimization and implementation of chemical processes. By focusing on reducing energy use, minimizing waste, utilizing renewable feedstocks and designing safer chemicals, AI-driven approaches promote sustainability across the chemical industry. AI optimizes reactions to minimize energy inputs, enabling energy-efficient practices essential to green chemistry. It also facilitates the use of renewable feedstocks and helps design processes that produce fewer harmful byproducts. Collaborative initiatives such as the open reaction database (ORD) illustrate the role of AI in enhancing green chemistry through the promotion of shared, open-access resources for sustainable synthesis. AI has also been instrumental in reducing energy requirements in discovering organic photovoltaic materials and scaling up green processes from lab research to industrial production, thus broadening the adoption of sustainable practices across industries [109-112]. Expanding on these AI applications will allow for continued progress in green chemistry, ensuring that AI-driven methodologies not only enhance efficiency and innovation but also align with the broader goals of sustainability and safety across industries.

Future perspectives: As AI continues to evolve, its potential for global adoption in green organic chemistry is immense. The integration of AI models in optimizing chemical reactions, designing eco-friendly materials and reducing waste aligns perfectly with global sustainability goals. However, widespread adoption of AI across laboratories and industries requires overcoming certain barriers.

One critical factor for global adoption is the accessibility of AI tools. To enable broader use, AI platforms must become more user-friendly, enabling chemists without advanced data science expertise to leverage these technologies. Furthermore, cloud-based AI systems can provide scalable solutions for laboratories and small businesses worldwide, reducing the need for substantial infrastructure investments. AI democratization will also require the development of open-access databases that are robust and well-curated, containing high-quality data relevant to green chemistry. Another essential consideration is the energy consumption of AI models themselves. While AI optimizes chemical processes to reduce environmental impacts, the computational power required to train certain models, particularly deep learning models, can be energy-intensive. Future developments should focus on enhancing the efficiency of AI algorithms, prioritizing models that balance environmental benefits with low energy use.

Regulatory challenges also present a key hurdle to AI-driven sustainable chemistry. Currently, there are no comprehensive global frameworks regulating the use of AI in chemical synthesis and green technologies. AI models, especially those that act as "black boxes" with opaque decision-making processes, may face scrutiny from regulatory bodies concerned with safety and transparency. Governments and international organizations need to establish regulatory guidelines that ensure AI's safe and ethical implementation in chemistry. These frameworks should include data protection, explainability requirements for AI models and safety standards to ensure AI-driven chemical processes do not inadvertently introduce environmental risks. Moreover, global collaboration will be crucial in addressing regulatory challenges and fostering innovation in AI for sustainable chemistry. Interdisciplinary partnerships involving chemists, AI researchers, policy makers and environmental agencies are necessary to develop global standards that encourage both innovation and safety. International forums such as the United Nations Environment Programme (UNEP) or World Economic Forum (WEF) could play pivotal roles in fostering cooperation, ensuring that AI technologies are adopted responsibly while promoting sustainability.

The future of AI in green chemistry holds great promise, but its global adoption will require overcoming challenges related to accessibility, energy efficiency and regulatory oversight. As AI continues to revolutionize sustainable chemistry, creating a structured framework for its ethical and responsible use will be essential for long-term environmental and societal benefits.

Conclusions

Artificial intelligence (AI) is reshaping the landscape of green organic chemistry by introducing innovative, data-driven solutions that significantly enhance the sustainability of chemical processes. Throughout this review, we have explored the ways AI optimizes reaction conditions, solvent selection, waste reduction and catalyst design, driving forward the goals of green chemistry. By leveraging ML algorithms and predictive models, AI enables more efficient, eco-friendly synthetic pathways, reducing both the environmental footprint and resource consumption associated with organic synthesis. While AI's transformative impact on green chemistry is clear, several challenges must be addressed to unlock its full potential. Data availability and quality remain critical issues, as many AI models rely on extensive, curated datasets, which are often sparse in the field of green chemistry. Additionally, the lack of transparency in AI models, often described as the "black box" problem, can create barriers to adoption by chemists who require understandable and interpretable results to guide their experimental work. These challenges highlight the need for ongoing interdisciplinary collaboration between chemists, data scientists and AI specialists to develop more practical, interpretable AI tools. Despite these obstacles, the future of AI in green organic chemistry is promising. AI-driven approaches are accelerating innovation in sustainable chemical research by optimizing reaction pathways, predicting safer solvents and catalysts and reducing harmful byproducts. As data-sharing initiatives grow and ML models become more sophisticated, AI will increasingly support the realization of 12 principles of green chemistry. Furthermore, AI's potential to scale up green chemistry innovations from the lab to industrial applications offers the prospect of widespread adoption of sustainable practices within the chemical industry. Consequently, AI holds the promise to transform our methodologies in organic synthesis and enhance our strategies for reducing the ecological footprint of chemical processes. As AI technologies continue to evolve, their integration into green chemistry will be instrumental in driving the transition toward a more sustainable and eco-friendly future for the chemical industry.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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