EJPMR, 2026, 13(11), 622-636 **Research Article** **Impact Factor: 8.158**

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

ISSN (O): 2394-3211

ISSN (P): 3051-2573

Coden USA: EJPMAG

AI-ASSISTED GREEN SYNTHESIS OF PHARMACEUTICAL COMPOUNDS: RECENT ADVANCES, APPLICATIONS, CHALLENGES AND FUTURE PERSPECTIVES

[1]Srushti Ashokkumar Naikwadi, *[2]Gaikwad S. D., [3]Wagh Anuradha Haribhau

[1]Student of Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra.
[2]Professor, Department of Pharmaceutical Chemistry, Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra.
[3]Student of Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra.

***Corresponding Author: Gaikwad S. D.**

Professor, Department of Pharmaceutical Chemistry, Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra.

DOI: https://doi.org/10.5281/zenodo.24127963

How to cite this Article: [1]Srushti Ashokkumar Naikwadi, *[2]Gaikwad S. D., [3]Wagh Anuradha Haribhau (2026). Ai-Assisted Green Synthesis Of Pharmaceutical Compounds: Recent Advances, Applications, Challenges And Future Perspectives. European Journal of Pharmaceutical and Medical Research, 13(11), 622–636.

This work is licensed under Creative Commons Attribution 4.0 International license.

Article Received on 15/10/2026 **Article Revised on 05/11/2026** **Article Published on 10/11/2026**

ABSTRACT

Pharmaceutical synthesis is a fundamental component of drug discovery and development, providing efficient routes for the preparation of active pharmaceutical ingredients and other therapeutically important compounds. However, conventional organic synthesis often relies on hazardous reagents, toxic solvents, excessive energy consumption, multi-step reactions, and generates substantial chemical waste, creating significant environmental, economic, and safety concerns. Green chemistry has emerged as an important approach to address these challenges by promoting the prevention of waste, improved atom economy, safer solvents and reagents, energy efficiency, catalysis, and the design of less hazardous chemical processes. The recent integration of artificial intelligence (AI) and machine learning (ML) with organic chemistry has created new opportunities to improve the sustainability and efficiency of pharmaceutical synthesis. AI- and ML-based models can analyse large chemical datasets and assist in predicting reaction outcomes, optimizing reaction conditions, selecting appropriate catalysts and solvents, and estimating reaction yields and selectivity. These approaches can reduce the number of experimental trials, consumption of chemicals, energy requirements, and overall waste generation during process development. Major applications include computer-assisted retrosynthetic analysis, reaction prediction, synthetic route optimization, catalyst and solvent selection, molecular and reaction-condition optimization, and AI-assisted automated synthesis of pharmaceutical compounds. The integration of AI with green chemistry can therefore support the development of shorter, safer, more economical, and environmentally sustainable synthetic routes for pharmaceuticals. Nevertheless, several challenges remain, including limited and biased datasets, data quality, model interpretability, prediction accuracy, computational requirements, experimental validation, scalability, and regulatory acceptance. Future developments are expected to focus on the integration of AI with automation, robotics, continuous-flow chemistry, real-time reaction monitoring, and sustainable-by-design approaches. This review highlights the role, applications, advantages, limitations, and future prospects of AI-assisted green synthesis in pharmaceutical chemistry.

KEYWORDS: Artificial Intelligence (AI); Machine Learning (ML); Green Chemistry; Pharmaceutical Synthesis; Organic Chemistry; Drug Synthesis; Sustainable Chemistry; Reaction Optimization; Retrosynthetic Analysis; Green Pharmaceutical Manufacturing.

INTRODUCTION

Pharmaceutical chemistry is an important field that combines chemistry, biology, and pharmaceutical sciences to develop and manufacture therapeutic compounds. The synthesis of pharmaceutical compounds involves the selection of suitable starting materials, chemical reactions, catalysts, solvents, and reaction conditions to obtain the desired product with high yield and purity. In recent years, increasing environmental concerns associated with conventional chemical synthesis have encouraged researchers to adopt the principles of green chemistry. At the same time,

advances in artificial intelligence (AI) and machine learning (ML) have created new opportunities to predict and optimize chemical reactions. The integration of AI with green chemistry has the potential to make pharmaceutical synthesis more efficient, economical, safe, and environmentally sustainable.

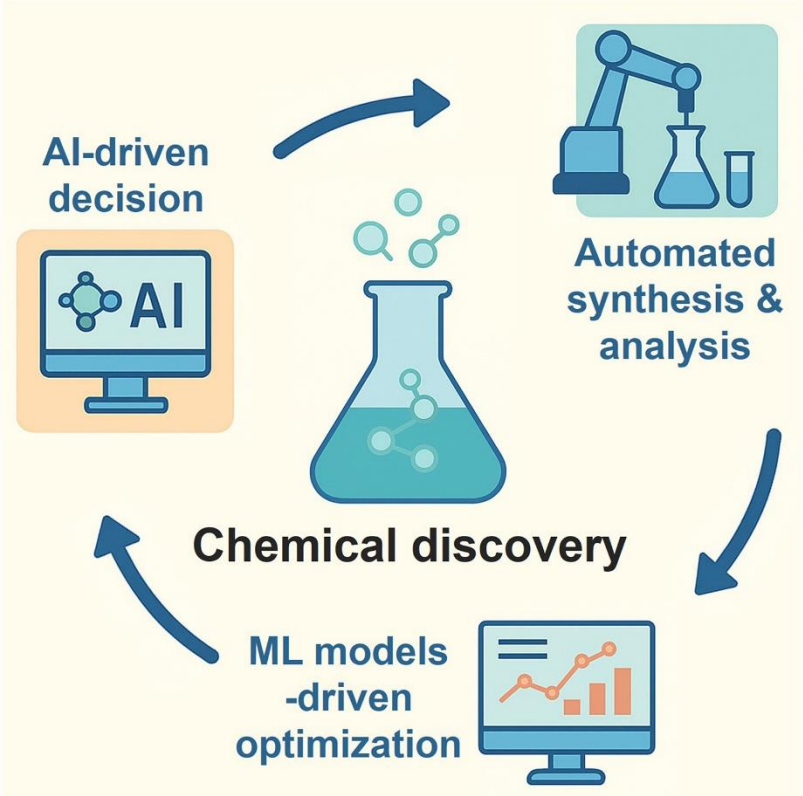


Fig: Chemical Discovery by using AI.

Chemical synthesis is the foundation of pharmaceutical development

Chemical synthesis enables researchers to prepare new drug candidates, modify existing molecules, and manufacture active pharmaceutical ingredients (APIs). During drug discovery, synthetic chemistry allows medicinal chemists to produce structural analogues of potential drug molecules and evaluate their biological activity. Once a promising compound is identified, the synthetic route must be further developed to obtain the compound with high purity, reproducibility, stability, and suitable production cost. Pharmaceutical synthesis may involve reactions such as oxidation, reduction, substitution, condensation, coupling, cyclization, and protection/deportation. The selection of a suitable synthetic pathway can strongly influence the overall efficiency, safety, cost, and environmental impact of pharmaceutical production.

Traditional synthesis depends heavily on experimental chemistry and optimization

Conventional pharmaceutical synthesis generally begins with the selection of starting materials and a proposed reaction pathway based on chemical knowledge, literature reports, and the experience of synthetic chemists. Researchers then select appropriate reagents, catalysts, solvents, temperature, reaction time, and other reaction parameters. Although traditional methods have been highly successful in producing pharmaceutical compounds, they often involve repeated laboratory experimentation. Multi-step synthetic routes can require optimization at every stage, increasing the consumption of chemicals, solvents, energy, and laboratory resources. This trial-and-error approach can therefore be time-consuming and costly.

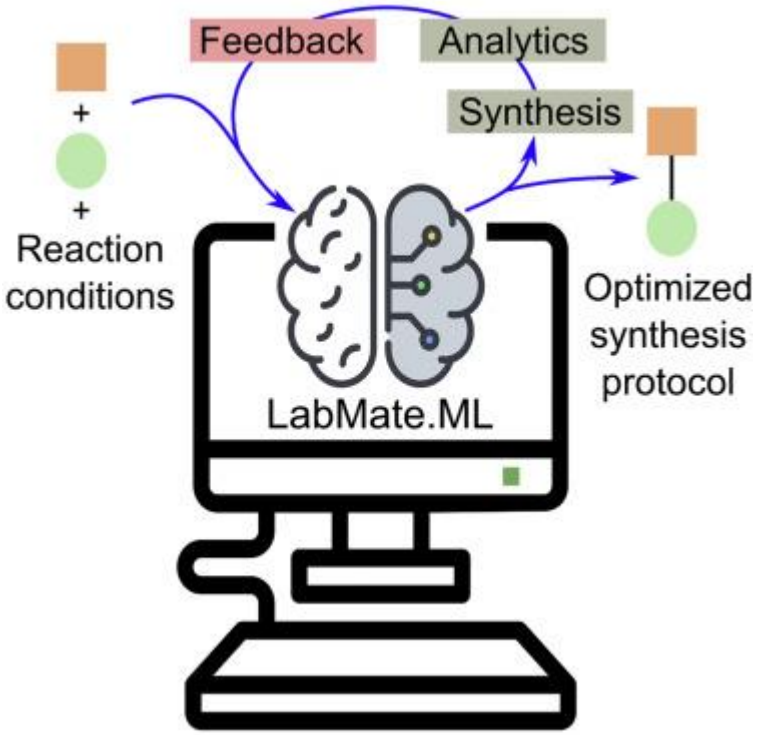


Fig: experimental chemistry and optimization.

Problems with Conventional Synthesis

Solvents are extensively used to dissolve reactants, control reaction conditions, and facilitate extraction and purification. However, several commonly used organic solvents are volatile, flammable, toxic, or environmentally harmful. Large-scale pharmaceutical manufacturing can therefore generate considerable solvent-related emissions and waste. Green synthesis encourages the replacement of hazardous solvents with safer alternatives or, where practical, the development of solvent-free reactions. AI-based solvent-selection approaches may further assist researchers in balancing reaction performance with environmental and safety considerations.

Hazardous reagents can create safety and environmental risks

Some conventional synthetic reactions require corrosive, toxic, highly reactive, or environmentally hazardous reagents. These substances may create risks during handling, transportation, storage, and disposal. They can also generate hazardous reaction by-products. Green chemistry seeks safer reagents and catalytic alternatives that can perform the desired transformation while reducing toxicity and waste. AI can assist in identifying and comparing suitable reagents and reaction pathways.

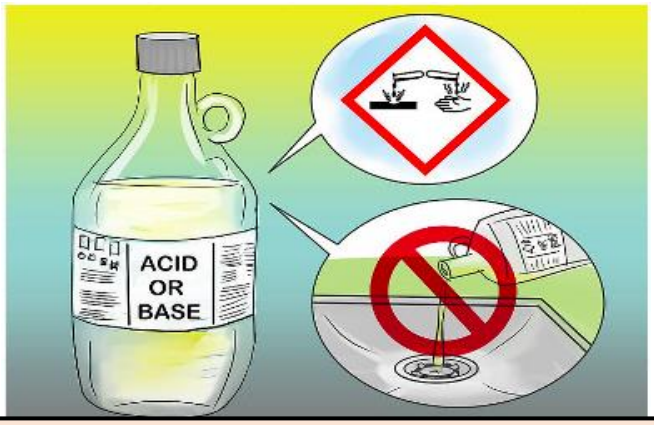


Fig: experimental chemistry and optimization.

Green chemistry seeks safer reagents and catalytic alternatives that can perform the desired transformation while reducing toxicity and waste. AI can assist in identifying and comparing suitable reagents and reaction pathways.

High Energy Consumption

Certain pharmaceutical reactions require prolonged heating, cooling, high pressure, or other energy-intensive conditions. These requirements increase energy consumption and can contribute to greenhouse-gas emissions depending on the energy source. Green chemistry promotes reactions that operate under mild conditions and require less energy. AI-assisted optimization can help identify reaction conditions that maintain performance while reducing reaction time and energy requirements.

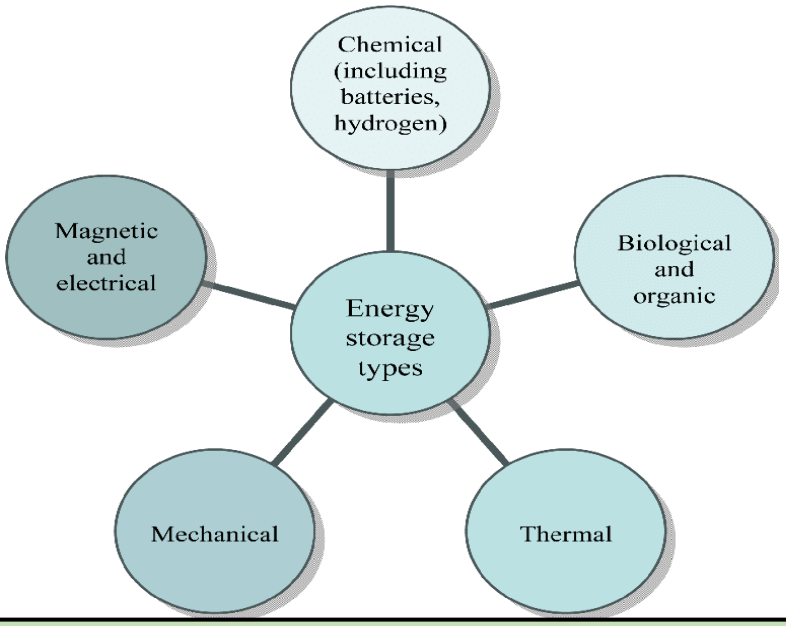


Fig: High Energy loss.

Conventional pharmaceutical synthesis can involve several environmental and processing challenges, including inefficient use of raw materials, hazardous reagents and solvents, high energy requirements, waste generation, and complex purification procedures. One important factor in evaluating the efficiency of a chemical reaction is atom economy, which describes how effectively the atoms present in the starting materials are incorporated into the desired final product. Reactions with poor atom economy generate larger quantities of unwanted by-products and consequently require greater quantities of raw materials. Improving atom economy can therefore reduce material consumption, waste generation, and production costs. In pharmaceutical synthesis, the selection of highly atom-efficient reactions is particularly important because complex drug molecules may require several synthetic steps. Another significant challenge is purification of the desired pharmaceutical compound**.** Following a chemical reaction, the product may need to be separated from unreacted starting materials, catalysts, solvents, and unwanted by-products. Conventional purification techniques such as extraction, crystallization, distillation, and chromatography may require considerable quantities of solvents and energy. Improving reaction conversion and selectivity can reduce impurity formation and simplify downstream purification, thereby improving both economic and environmental efficiency. The cumulative consumption of raw materials, solvents, water, and energy, together with the generation of waste and hazardous substances, contributes to the overall environmental footprint of pharmaceutical manufacturing. Therefore, modern pharmaceutical synthesis increasingly focuses on developing processes that maintain product quality while minimizing environmental impact. Green chemistry provides a systematic approach to achieving these objectives. It focuses on the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances. The 12 principles of green chemistry provide a framework for designing safer and more sustainable chemical processes. Important principles for pharmaceutical synthesis include waste prevention, atom economy, less hazardous chemical synthesis, safer solvents and auxiliaries, energy efficiency, catalysis, and the use of renewable feedstock's.

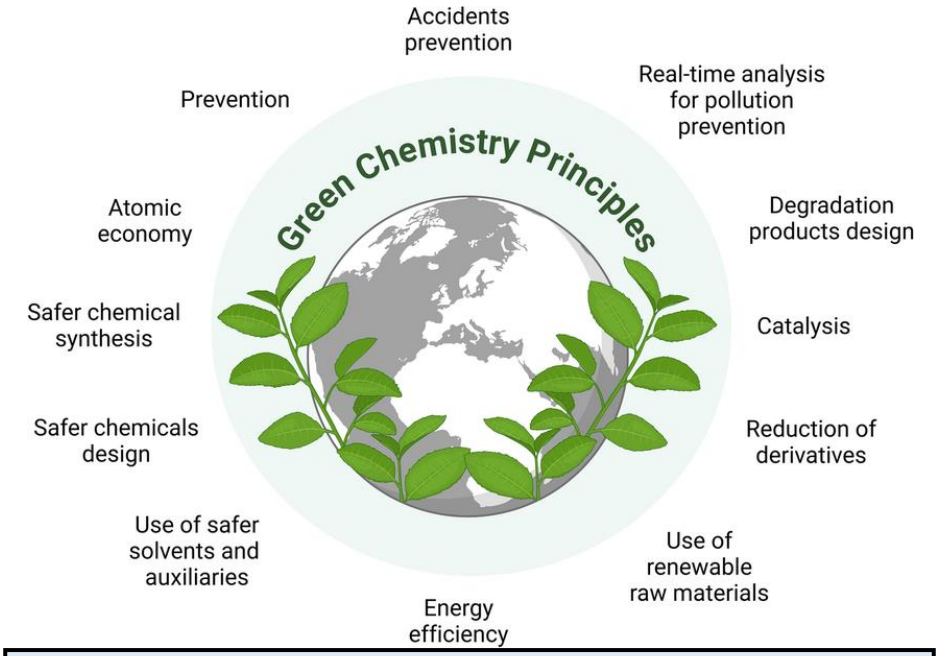


Fig: Principle of Green Chemistry.

AIM OF THE REVIEW

This review aims to summarize recent advances in the application of artificial intelligence (AI) for the design, prediction, and optimization of environmentally sustainable synthetic routes for pharmaceutical compounds. It highlights how AI-driven approaches can facilitate the selection of safer reagents, solvents, catalysts, and reaction conditions while minimizing waste generation, energy consumption, and the use of hazardous materials. Particular emphasis is placed on machine learning, deep learning, and data-driven reaction prediction methods that enable efficient route planning, reaction outcome prediction, and process optimization. The review also discusses the potential of AI to integrate principles of green chemistry into pharmaceutical synthesis, thereby supporting the development of safer, more efficient, cost-effective, and environmentally responsible manufacturing processes.

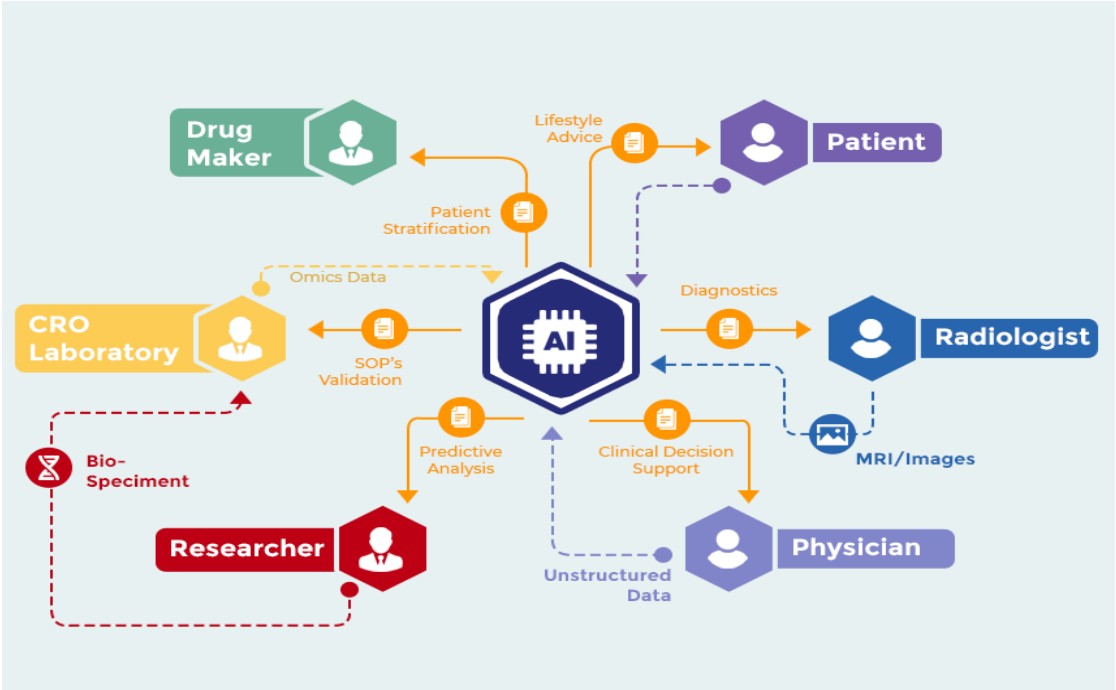


Fig: Use of Ai and Programing.

This review explains how AI can help design greener and safer methods for making pharmaceutical compounds. Reduce waste, energy use, toxicity, and environmental impact in pharmaceutical synthesis.

Application of AI in Pharmaceutical Green Chemistry

1. Small-Molecule Pharmaceuticals

AI-based reaction prediction and retrosynthetic planning are increasingly used for the synthesis of small-molecule drug candidates. Machine-learning models can analyse previous reaction data and predict suitable reaction conditions, catalysts, bases, and solvents.
Example: Suzuki coupling in medicinal chemistry

AI technique: Machine learning/geometric deep learning.

Reaction: Suzuki C–C cross-coupling.

Green approach: AI-assisted selection of catalyst–solvent–base combinations and reduction of unnecessary experimental screening.

Key outcome: The model achieved 76.3% accuracy for three-category reaction classification and successfully supported condition selection for new coupling reactions.
Significance: By reducing trial-and-error experiments, AI can decrease solvent, reagent, and energy consumption during pharmaceutical development.

2. Heterocyclic Compounds

Heterocyclic structures are present in a large proportion of pharmaceutical molecules. AI can assist in selecting efficient synthetic routes and reaction conditions for heterocyclic formation.

Example: Heterocyclic synthesis using computer-aided retro synthesis.

AI technique: Computer-aided retro synthesis (CAR).

Reaction: Heterocyclic-forming reactions, including thiazide synthesis.

Green approach: Route selection based on fewer operations, improved reaction efficiency, and integration with continuous-flow processing.

Key outcome: A recent study used CAR to identify a common Hantzsch thiazole synthesis applicable to 11 different APIs. Continuous-flow optimization gave a 95% isolated yield and improved the Green Motion score by 25%. Science Direct.

Significance: Combining AI route planning with flow chemistry can improve yield while reducing resource consumption.

AI can improve pharmaceutical synthesis by predicting efficient reactions, optimizing conditions, and reducing unnecessary experimentation. Overall, its integration with green chemistry and flow processes can enhance yield, efficiency, and sustainability while reducing waste and resource consumption. Yes. These two examples show that AI is useful in green and AI-assisted green chemistry synthesis by helping chemists select efficient reaction conditions, reduce trial-and-error experiments, and design shorter synthetic routes.

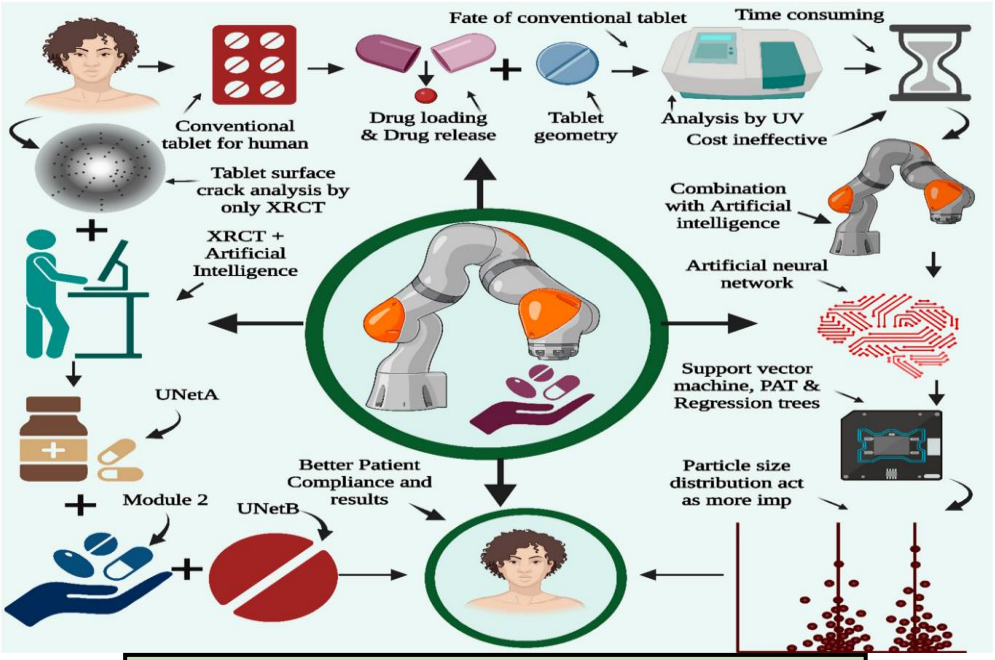


Fig: Application of AI.

AI Tools and Platforms Used in Chemical Synthesis

I. Reaction Prediction Models

Reaction prediction models use artificial intelligence and machine learning to predict the likely products and outcomes of chemical reactions. These models are trained using large databases of previously reported reactions and can help researchers select suitable reagents, catalysts, solvents, and reaction conditions. In pharmaceutical synthesis, they reduce trial-and-error experimentation and support faster development of efficient and greener reactions.

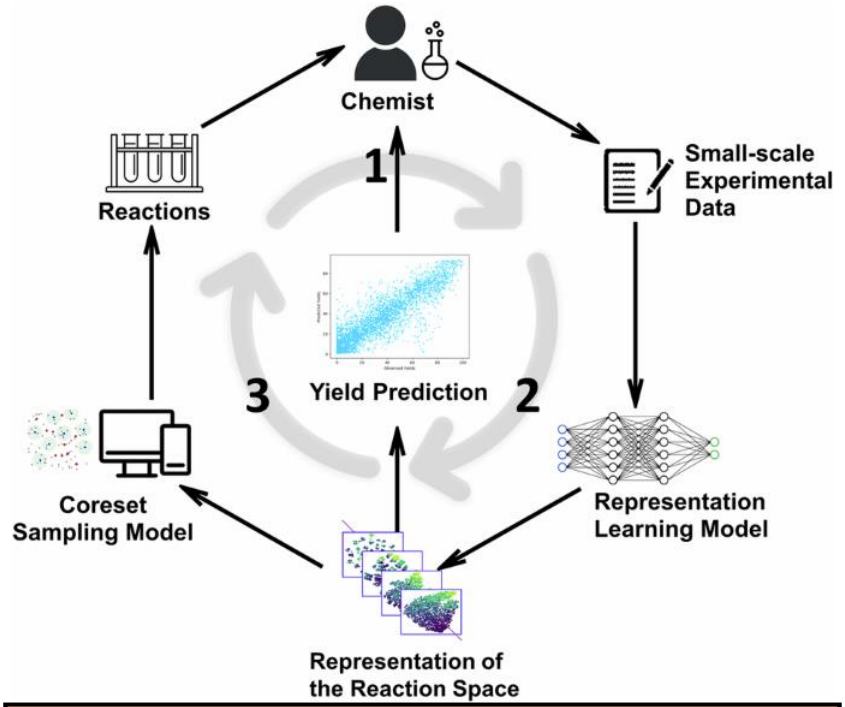


Fig: Reaction Prediction Models.

II. IBM RXN for Chemistry

It is an AI-based platform developed by IBM Research that helps predict chemical reactions and synthetic pathways. It uses machine-learning models trained on large collections of chemical reactions to predict the products that may form from given reactants. The platform can also assist with retro synthesis, where a complex target molecule is broken down into simpler starting materials. It is useful in organic chemistry, pharmaceutical research, and drug development because it allows chemists to explore possible reactions before performing laboratory experiments.

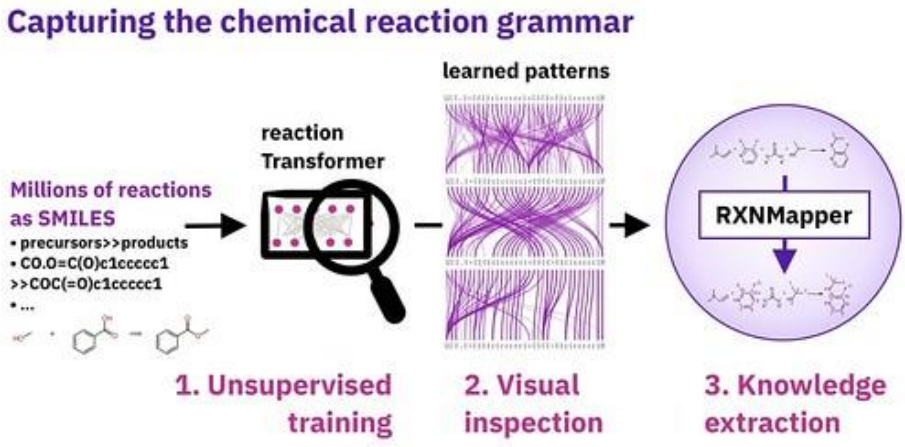


Fig: IBM RXN for chemistry.

III. Molecular Transformer

It is a deep-learning model designed to predict the outcome of chemical reactions. It uses chemical structures represented as SMILES strings and applies a Transformer-based architecture to learn relationships between reactants and products. It can be used for reaction prediction, retro synthesis, and synthesis planning. The main advantage of Molecular Transformer is its ability to analyse large numbers of chemical reactions quickly, helping researchers identify potentially useful reactions and synthetic pathways.

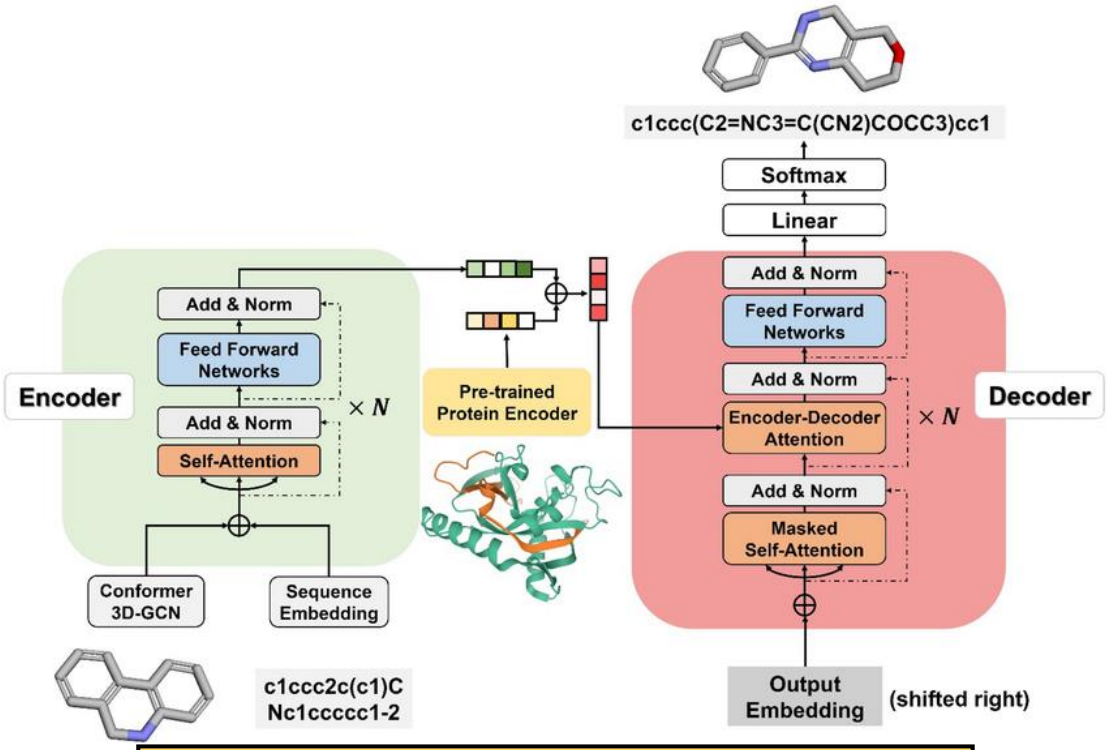


Fig: Molecular Transformer.

IV. ASKCOS (Automated System for Knowledge-based Synthesis Planning)

It is an open-source platform developed at MIT for computer-assisted chemical synthesis planning. It uses reaction databases and machine-learning models to work backward from a target molecule and suggest possible synthetic routes. ASKCOS can provide several alternative pathways, which allows chemists to compare routes based on factors such as reaction availability and complexity. It is particularly useful in pharmaceutical and organic chemistry research. The platform uses previously reported chemical reactions to improve the reliability of its predictions. ASKCOS is particularly useful for planning the synthesis of complex organic molecules and pharmaceutical compounds. It can reduce the time researchers spend manually searching through reaction databases and scientific literature. Experiments.

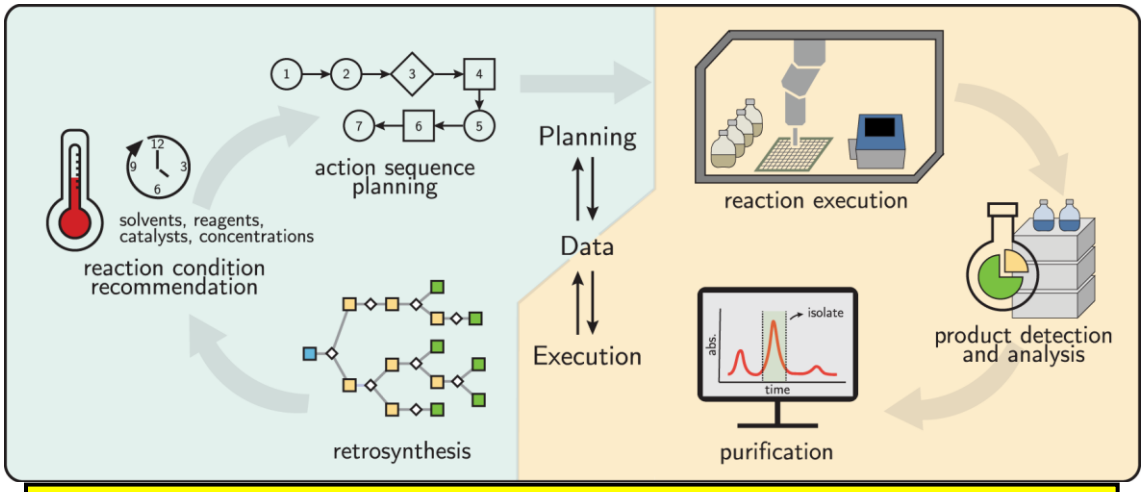


Fig: Automated System for Knowledge-based Synthesis Planning.

V. Chemistry42

It is an AI-powered molecular design platform used mainly in drug discovery and molecular optimization. It can generate new chemical structures according to desired properties, such as biological activity, selectivity, or physicochemical characteristics. The platform combines different AI methods to explore large chemical spaces and identify promising molecules. This can help researchers design potential drug candidates and optimize their structures before synthesis and testing.

Overall, these AI tools make chemical synthesis more efficient, faster, and data-driven. They assist chemists in predicting reactions, discovering new molecules, and selecting suitable synthetic routes. However, AI predictions still need to be evaluated by chemists and confirmed through laboratory experiments.

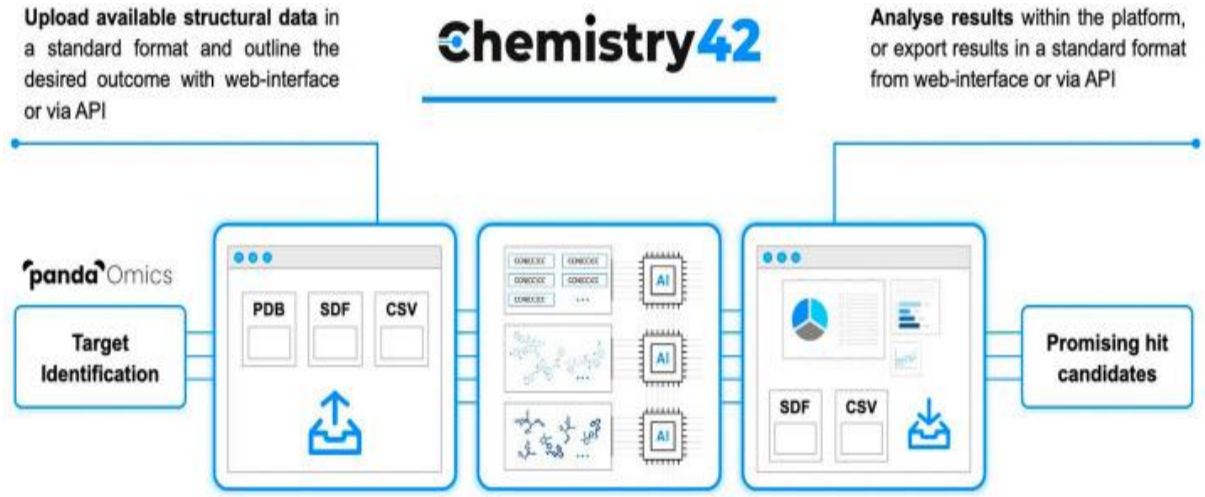


Fig: Chemistry42.

Challenges of AI-Assisted Green Synthesis of Pharmaceutical Compounds

1. Limited and Poor-Quality Data

AI models used in chemical synthesis depend on large amounts of accurate, reliable, and well-organized chemical data for training. However, many chemical reaction datasets contain incomplete information about reactants, products, reaction conditions, yields, solvents, and catalysts. Data may also be reported in different formats or contain errors and duplicate information. This makes it difficult for AI systems to learn chemical relationships correctly. Poor-quality or limited data can therefore lead to inaccurate reaction predictions and unsuitable synthetic routes. In addition, many newly developed pharmaceutical reactions may not yet be available in public databases. Improving the quality, standardization, and availability of chemical data is therefore an important challenge for developing reliable AI-assisted green synthesis methods.

2. Lack of Experimental Validation

AI systems can predict chemical reactions and suggest possible synthetic pathways, but these predictions cannot be considered completely reliable without laboratory testing. A reaction may appear highly suitable based on computational models but may fail under actual experimental conditions. Factors such as temperature, pressure, reaction time, solvent, catalyst concentration, impurities, and mixing can affect the reaction outcome. AI models may also predict a good product yield without fully considering unexpected side reactions or the formation of unwanted by-products. Therefore, each AI-generated synthetic route must be experimentally tested and optimized by chemists. This process can require significant time, resources, and laboratory materials. Experimental validation is particularly important in pharmaceutical synthesis, where product purity, safety, and reproducibility are essential. Combining AI predictions with laboratory experiments can improve the reliability and practical usefulness of AI-assisted synthesis.

3. Complexity of Pharmaceutical Synthesis

Pharmaceutical synthesis is often a complex process that requires several chemical reactions to produce the desired compound. Each step may involve different reactants, catalysts, solvents, temperatures, and reaction conditions. The formation of complex intermediates can make it difficult for AI models to accurately predict the complete synthetic pathway. In addition, unwanted side reactions may occur and produce impurities or by-products that are difficult to predict. Small changes in reaction conditions can also significantly affect the yield, selectivity, and purity of the final product. AI models trained on existing reaction data may not fully understand these complex chemical interactions. Multi-step synthesis also increases the possibility of errors because an incorrect prediction at one stage can affect all subsequent steps. Therefore, developing AI systems capable of accurately handling complex, multi-step pharmaceutical synthesis remains a major challenge. Combining AI predictions with expert chemical knowledge and experimental validation is essential for obtaining reliable results.

4. Evaluation of Green Chemistry

An AI-designed synthesis route may be fast, efficient, and capable of producing a high yield, but this does not always mean that the process is environmentally friendly. Green synthesis requires the evaluation of several environmental and safety factors. The toxicity and environmental impact of solvents, reagents, catalysts, and by-products must be considered before selecting a synthetic route. AI systems should also evaluate the amount of chemical waste generated during the reaction and the atom economy, which indicates how efficiently reactant atoms are incorporated into the final product. Energy consumption is another important factor, especially when reactions require high temperatures, high pressure, or long reaction times. The use of renewable materials and safer solvents should also be considered. However, many current AI models focus mainly on reaction yield and product prediction rather than overall environmental impact. Therefore, integrating green chemistry principles into AI models is necessary to design pharmaceutical synthesis routes that are not only efficient but also safe, sustainable, and environmentally responsible.

5. High Computational Requirements

Advanced AI models used in chemical synthesis often require powerful computing systems, large chemical databases, and specialized software to process and analyse complex chemical information. Training these models can involve large amounts of data and require significant computational power, memory, and storage. This can increase the cost of developing and operating AI-based synthesis systems. Small laboratories, universities, and research institutions may not have access to high-performance computers or the necessary technical infrastructure. In addition, maintaining chemical databases and updating AI models requires continuous resources and technical expertise. Cloud-based computing can provide an alternative, but it may also involve subscription or data-processing costs.

Future Perspectives of AI-Assisted Green Synthesis of Pharmaceutical Compounds

1. Development of More Accurate AI Models

In the future, AI models are expected to become more accurate and reliable in predicting chemical reactions, product yields, selectivity, and suitable reaction conditions. Improvements in machine learning and deep learning techniques will allow AI systems to learn from larger and higher-quality chemical datasets. These models may be able to better understand complex chemical interactions and predict possible side reactions and impurities. AI could also recommend suitable catalysts, solvents, temperatures, and reaction times for specific pharmaceutical synthesis processes. More accurate predictions will reduce the number of unsuccessful laboratory experiments and save chemicals, time, and resources. AI models may also compare different synthetic pathways and identify the most efficient and environmentally friendly route. Improved accuracy will increase the confidence of chemists in using AI for synthesis planning. Ultimately, the development of advanced AI models could support **faster,** safer, more economical, and greener pharmaceutical synthesis.

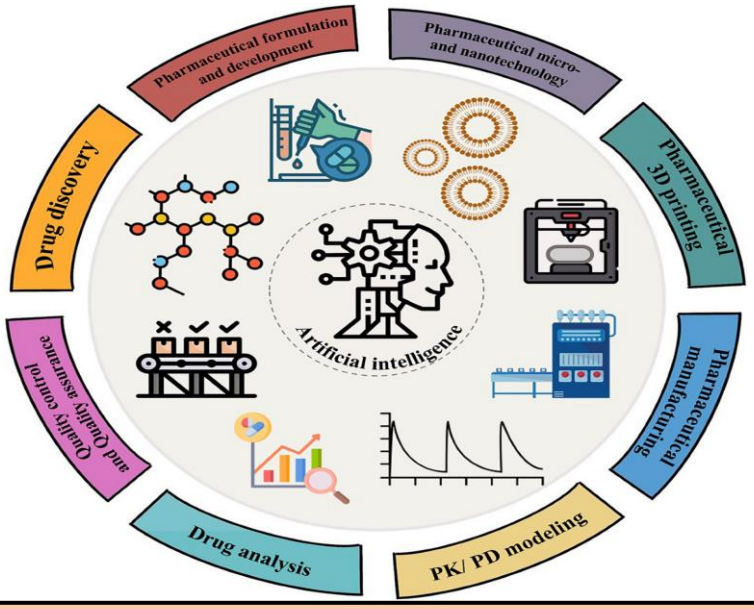


Fig: Development of More Accurate AI Models.

2. Integration of Green Chemistry Principles

In the future, AI tools are expected to integrate green chemistry principles directly into the design of pharmaceutical synthesis pathways. Instead of focusing only on reaction yield and efficiency, AI systems can evaluate the environmental impact of different reactions. They may recommend safer and less toxic solvents, catalysts, and reagents to reduce risks to human health and the environment. AI can also identify synthetic routes that produce less chemical waste and require fewer reaction steps. Another important goal is to improve atom economy, ensuring that a greater proportion of the starting materials is incorporated into the final pharmaceutical product. AI systems may also select reactions that require lower temperatures, lower pressure, and less energy. In addition, renewable raw materials and recyclable catalysts could be considered during synthesis planning. By combining reaction prediction with environmental assessment, AI can help chemists develop pharmaceutical processes that are both effective and sustainable. This integration could significantly contribute to safer, cleaner, and more environmentally friendly pharmaceutical manufacturing.



Fig: Integration of Green Chemistry Principles.

3. Automated Synthesis and Robotics

In the future, AI can be integrated with laboratory robotics and automated synthesis equipment to create more efficient and intelligent chemical research workflows. AI systems can first design a suitable reaction pathway and select appropriate reactants, solvents, catalysts, and reaction conditions. Automated laboratory robots can then perform the experiments with minimal human intervention. Analytical instruments can monitor the reactions and provide information about product formation, yield, purity, and reaction progress. The experimental results can be automatically sent back to the AI system for analysis. Based on these results, the AI can modify the reaction conditions and conduct further experiments to improve the outcome. This repeated process, known as automated or self-optimizing experimentation, can significantly reduce the time required for reaction optimization. It can also reduce human error and minimize the unnecessary use of chemicals and laboratory resources. In pharmaceutical research, AI-driven robotic systems could accelerate the discovery and development of new drug compounds. Overall, combining AI with robotics has the potential to make chemical synthesis faster, more precise, efficient, and sustainable**.**

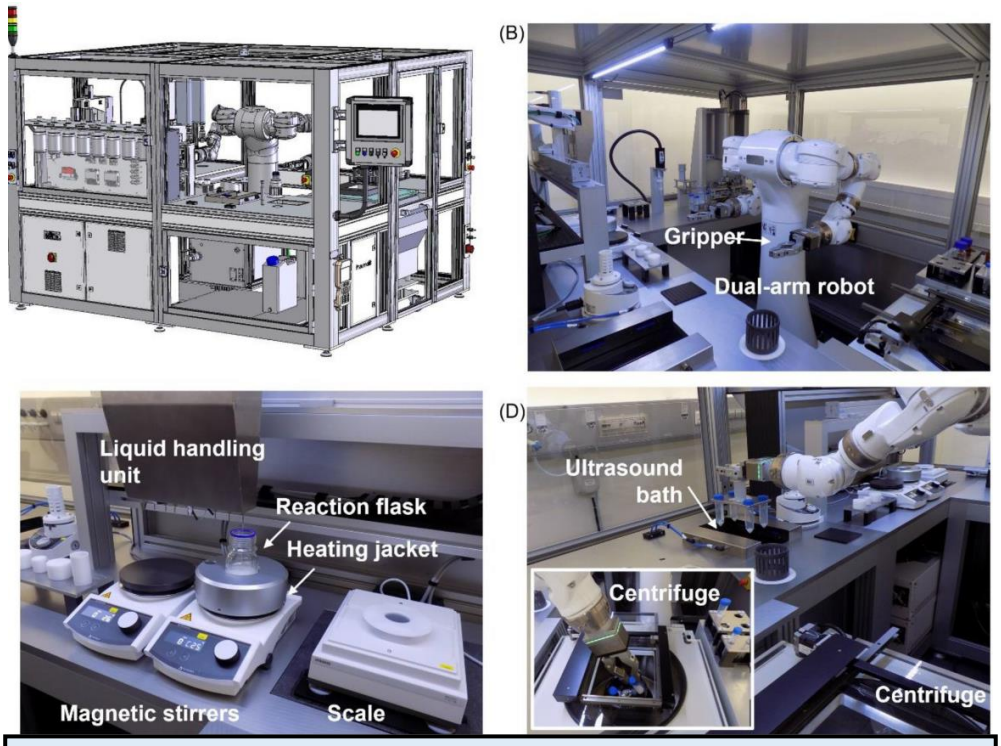


Fig: Automated Synthesis and Robotics.

RESULT

The review of recent studies indicates that artificial intelligence (AI) has become an effective tool for improving the efficiency and sustainability of pharmaceutical synthesis. AI-assisted route design enables the prediction of suitable retrosynthetic pathways and identification of shorter and more efficient synthetic routes. By reducing the number of synthetic steps, these approaches can decrease the consumption of reagents and solvents and improve overall process efficiency.AI and machine learning (ML) techniques have also shown significant potential in optimizing reaction conditions. Important parameters such as temperature, reaction time, solvent, catalyst concentration, and reagent ratio can be predicted and optimized using data-driven models. This reduces the requirement for repeated experimental trials and can improve reaction yield, selectivity, and reproducibility.

The integration of AI with green chemistry principles has further contributed to the reduction of waste and hazardous chemical use. AI-based systems can assist in selecting synthetic pathways involving safer solvents, less hazardous reagents, and more efficient reactions. Consequently, improvements can be achieved in important green chemistry parameters such as atom economy, E-factor, process mass intensity, and overall environmental performance. AI-assisted approaches have also been applied to the sustainable synthesis of pharmaceutical intermediates, active pharmaceutical ingredients, heterocyclic compounds, and chiral molecules. The combination of AI with emerging technologies such as flow chemistry, photo catalysis, electrochemistry, and biocatalysts provides additional opportunities for developing efficient and environmentally sustainable pharmaceutical processes. Despite these advantages, several challenges remain in

the implementation of AI-assisted green synthesis. These include the availability and quality of chemical datasets, inconsistent experimental data, limited interpretability of some AI models, computational requirements, difficulties in scaling laboratory reactions to industrial production, and the lack of standardized methods for evaluating the environmental benefits of AI-based synthetic processes. Addressing these challenges will be essential for the wider adoption of AI-assisted green pharmaceutical synthesis.

DISCUSSION

The findings of this review demonstrate that the integration of artificial intelligence (AI) with green chemistry has considerable potential to transform pharmaceutical synthesis. AI-assisted route design can help chemists identify efficient retrosynthetic pathways and reduce unnecessary synthetic steps. Shorter synthetic routes can decrease the consumption of solvents, reagents, energy, and other resources, thereby contributing to more sustainable pharmaceutical manufacturing. The optimization of reaction conditions is another important advantage of AI-assisted synthesis. Machine learning models can analyse large amounts of experimental data and identify suitable combinations of temperature, reaction time, solvent, catalyst, and reagent concentration. This can reduce the number of experiments required during process development and improve reaction yield and selectivity. Therefore, AI can make the optimization process faster while potentially reducing laboratory waste and resource consumption.

The use of AI also supports the principles of green chemistry by helping researchers select safer and more sustainable chemicals and reaction pathways. Parameters such as atom economy, E-factor, and process mass intensity can be incorporated into route evaluation to compare the environmental performance of different synthetic approaches. However, achieving a high reaction yield alone does not necessarily indicate that a process is environmentally sustainable. A complete assessment should also consider solvent toxicity, energy consumption, waste generation, water use, and the overall life-cycle impact of the process. The combination of AI with emerging technologies such as flow chemistry, photo catalysis, electrochemistry, and biocatalysts provides further opportunities for sustainable pharmaceutical synthesis. AI can optimize these advanced processes and identify suitable operating conditions, while the technologies themselves can reduce energy consumption, hazardous reagents, and waste generation. This synergistic approach may be particularly useful for the development of efficient and scalable pharmaceutical manufacturing processes.

Despite these promising advantages, several limitations need to be addressed. The performance of AI models strongly depends on the quality, quantity, and consistency of available chemical data. Incomplete or biased datasets can lead to inaccurate predictions. In addition, some AI models operate as black boxes, making it difficult for chemists to understand the reasons behind their predictions. Scaling an AI-optimized reaction from laboratory conditions to industrial production is another major challenge because reaction behavior can change with differences in mixing, heat transfer, mass transfer, and equipment.

Overall, the discussion indicates that AI should be considered as a complementary tool rather than a replacement for chemical expertise. The most effective approach is likely to involve collaboration between AI models, experimental chemists, automated laboratory systems, and green chemistry principles. Future developments should focus on improving data quality, model transparency, sustainability metrics, and experimental validation to achieve reliable and environmentally responsible pharmaceutical synthesis.

CONCLUSION

The integration of artificial intelligence (AI) with green chemistry represents a promising approach for developing more sustainable pharmaceutical synthesis processes. AI-assisted route design can identify efficient synthetic pathways, while machine learning can optimize reaction conditions and improve yield, selectivity, and process efficiency. These approaches can also contribute to reducing solvent consumption, hazardous chemical use, waste generation, and energy requirements. The combination of AI with advanced technologies such as flow chemistry, photo catalysis, electrochemistry, and biocatalysts further expands its potential in sustainable pharmaceutical manufacturing. However, challenges related to data quality, model transparency, computational requirements, industrial scale-up, and standardized green chemistry metrics still need to be addressed. In conclusion, AI-assisted green synthesis has the potential to shift pharmaceutical development from conventional trial-and-error methods toward more predictive, efficient, and environmentally sustainable processes. Continued collaboration among chemists, AI researchers, pharmaceutical industries, and green chemistry experts will be essential for translating these advances into practical large-scale applications. Future research should focus on developing reliable, explainable, and sustainability-focused AI systems that can support safer and greener pharmaceutical manufacturing.

ACKNOWLEDGEMENT

I would like to express my sincere gratitude to Samarth Institute of Pharmacy, Belhe, Junnar, Pune, Maharashtra, for providing me with the opportunity, facilities, and academic support required to complete this review paper. I am deeply thankful to my respected guide, Dr. Shital Gaikwad Ma'am**,** for her valuable guidance, continuous support, encouragement, and constructive suggestions throughout the preparation of this review paper. I would also like to express my sincere gratitude to the Principal, Head of the Department (HOD), Academic In-charge,

teaching staff, and non-teaching staff of Samarth Institute of Pharmacy for their valuable support and encouragement. I am also thankful to all the scientists, researchers, and authors whose valuable research and published work on AI-assisted green synthesis of pharmaceutical compounds provided important information and contributed to the completion of this review. Finally, I would like to express my heartfelt thanks to each and every person who directly or indirectly helped, supported, and encouraged me during the preparation of this review paper. Their cooperation and support are sincerely appreciated.

REFERENCES

1. Segler, M. H. S., Preuss, M., & Waller, M. P. (2018). Planning chemical syntheses with deep neural networks and symbolic AI. *Nature*, *555*(7698): 604–610. https://doi.org/10.1038/nature25978
2. Granda, J. M., Donina, L., Dragone, V., Long, D. L., & Cronin, L. (2018). Controlling an organic synthesis robot with machine learning to search for new reactivity. *Nature*, *559*(7714): 377–381. https://doi.org/10.1038/s41586-018-0307-8
3. Coley, C. W., Jin, W., Rogers, L., Jamison, T. F., Jaakkola, T. S., Green, W. H., et al. (2019). A graph-convolutional neural network model for the prediction of chemical reactivity. *Chemical Science*, *10*(2): 370–377. https://doi.org/10.1039/C8SC04228D
4. Schwaller, P., Laino, T., Gaudin, T., Bolgar, P., Hunter, C. A., Bekas, C., et al. (2019). Molecular Transformer: A model for uncertainty-calibrated chemical reaction prediction. *ACS Central Science*, *5*(9): 1572–1583. https://doi.org/10.1021/acscentsci.9b00576
5. Lee, A. A., Yang, Q., Sresht, V., Bolgar, P., Hou, X., Klug-McLeod, J. L., et al. (2019). Molecular Transformer unifies reaction prediction and retrosynthesis across pharma chemical space. *Chemical Communications*, *55*: 12152–12155. https://doi.org/10.1039/C9CC05122H
6. Schwaller, P., Petraglia, R., Zullo, V., Nair, V. H., Haeuselmann, R. A., Pisoni, R., et al. (2020). Predicting retrosynthetic pathways using transformer-based models and a hyper-graph exploration strategy. *Chemical Science*, *11*: 3316–3325. https://doi.org/10.1039/C9SC05704H
7. Genheden, S., Thakkar, A., Chadimová, V., Reymond, J. L., Engkvist, O., & Bjerrum, E. (2020). AiZynthFinder: A fast, robust and flexible open-source software for retrosynthetic planning. *Journal of Cheminformatics*, *12*: 70. https://doi.org/10.1186/s13321-020-00472-1
8. Burger, B., Maffettone, P. M., Gusev, V. V., Aitchison, C. M., Bai, Y., Wang, X., et al. (2020). A mobile robotic chemist. *Nature*, *583*: 237–241. https://doi.org/10.1038/s41586-020-2442-2
9. Pesciullesi, G., Schwaller, P., Laino, T., & Reymond, J. L. (2020). Transfer learning enables the molecular transformer to predict regio- and stereoselective reactions on carbohydrates. *Nature Communications*, *11*: 4874. https://doi.org/10.1038/s41467-020-18671-7
10. Shields, B. J., Stevens, J., Li, J., Parasram, M., Damani, F., Alvarado, J. I. M., et al. (2021). Bayesian reaction optimization as a tool for chemical synthesis. *Nature*, *590*: 89–96. https://doi.org/10.1038/s41586-021-03213-y
11. Wang, Y., Li, W., Yang, J., et al. (2022). The roles of computer-aided drug synthesis in drug development. *Green Synthesis and Catalysis*, *3*(1): 11–24.
12. Kar, S., Sanderson, H., Roy, K., Yoshioka, N., Gutsch, D., Cerniglia, C. E., et al. (2022). Green chemistry in the synthesis of pharmaceuticals. *Chemical Reviews*, *122*(3): 3637–3710. https://doi.org/10.1021/acs.chemrev.1c00631
13. Hessel, V., Tran, N. N., Asrami, M. R., Tran, Q. D., Long, N. V. D., Escribà-Gelonch, M., et al. (2022). Sustainability of green solvents—Review and perspective. *Green Chemistry*, *24*: 410–437. https://doi.org/10.1039/D1GC03662A
14. Guo, J., Ranković, B., & Schwaller, P. (2023). Bayesian optimization for chemical reactions. *CHIMIA*, *77*(1–2): 31–38. https://doi.org/10.2533/chimia.2023.31
15. White, A. D. (2023). The evolution of chemistry with artificial intelligence. *Nature Reviews Chemistry*, *7*: 457–458.
16. Struble, T. J., Saldanha, F. A., Cosler, D. J., et al. (2020). Current and future roles of artificial intelligence in medicinal chemistry synthesis. *Drug Discovery Today*, *25*(9): 1730–1740.
17. Artificial Intelligence Methods and Models for Retro-Biosynthesis: A Scoping Review. (2024). *ACS Synthetic Biology*, *13*(8): 2276–2294.
18. Ahmad, S., Jaiswal, R., Yadav, R., & Verma, S. (2024). Recent advances in green chemistry approaches for pharmaceutical synthesis. *Sustainable Chemistry One World*, *4*: 100029.
19. Pharmaceutical advances: Integrating artificial intelligence in QSAR, combinatorial and green chemistry practices. (2024). *Intelligent Pharmacy*, *2*(5): 598–608.
20. Wei, Y., Shan, L., Qiu, T., Lu, D., & Liu, Z. (2025). Machine learning-assisted retrosynthesis planning: Current status and future prospects. *Chinese Journal of Chemical Engineering*, *77*: 273–292.
21. Yadav, S., Chandra, H., Tiwari, K. S., Bharty, M. K., Chandravanshi, R., Chauhan, D. S., et al. (2026). A review on the role of artificial intelligence and data science in green and sustainable chemistry: Current trends and futuristic pathways. *Discover Chemical Engineering*, *6*: 1.
22. Gangwal, A., & Lavecchia, A. (2026). AI-driven synthesis in medicinal chemistry: Integrating large language models, robotic automation, and

sustainability metrics to accelerate drug discovery. *Medicinal Research Reviews*.
23. Gaikwad, A. S. (2026). Green organic synthesis in drug discovery: Emerging roles of artificial intelligence and quantum chemical approaches. *Discover Chemistry*, *3*: 330.
24. Sheldon, R. A. (2018). Metrics of green chemistry and sustainability: Past, present, and future. *ACS Sustainable Chemistry & Engineering*, *6*(1): 32–48. https://doi.org/10.1021/acssuschemeng.7b03505.