EDUZONE: International Peer Reviewed/Refereed Multidisciplinary Journal (EIPRMJ),
ISSN: 2319-5045 Volume 14, Issue 2, July-December, 2025, Available online at: www.eduzonejournal.com

Green Organic Synthesis for Sustainable Drug Development

Pooja

Email- poojadahiya459@gmail.com

ABSTRACT

By incorporating green chemistry concepts into its production procedures, the pharmaceutical sector is placing a greater emphasis on sustainable development. This review looks at different green synthesis techniques used in pharmaceutical manufacturing, with an emphasis on how they might lessen their negative effects on the environment while increasing the effectiveness of drug synthesis. Important tactics are thoroughly examined, including the utilisation of green solvents and catalysts, biocatalysis, and plant-mediated synthesis. Successful case studies are also included in the article, such as the environmentally friendly synthesis of common medications like atorvastatin and ibuprofen. Even though there has been a lot of development, issues including cost concerns, regulatory obstacles, and scalability still exist. The benefits of green chemistry in pharmaceutical manufacturing are discussed in this study, with a focus on how it reduces waste, energy use, and the use of dangerous chemicals. Promising opportunities for attaining both environmental sustainability and economic viability are presented by the integration of green synthesis into conventional pharmaceutical manufacture.

Keywords: sustainable production, biocatalysis, green synthesis, green chemistry, pharmaceutical business

INTRODUCTION

The pharmaceutical sector, which is essential to the development of global healthcare, is coming under increasing pressure to reduce its environmental impact while preserving high standards of medication production quality and productivity. Conventional manufacturing methods sometimes rely on dangerous solvents, poisonous chemicals, and wasteful energy use, all of which present serious environmental dangers. This has prompted researchers to look for more environmentally acceptable and sustainable substitutes using the concepts of green chemistry. While encouraging the use of renewable resources and energy-efficient procedures, green synthesis strategies in pharmaceutical manufacture place an emphasis on cutting waste, energy use, and the use of hazardous chemicals. By using less hazardous chemicals, reducing byproducts, and increasing overall process efficiency, green chemistry in pharmaceutical manufacture aims to improve sustainability. One notable area of study is biocatalysis, where enzymes or microorganisms substitute hazardous chemicals as catalysts, enabling the selective and efficient manufacture of medications. In order to minimise environmental damage while preserving or even increasing synthesis yields, the development of green solvents and catalytic systems is also essential. With an emphasis on biocatalysis, nanoparticle synthesis, and environmentally friendly catalytic systems, this review examines recent developments in green synthesis in the pharmaceutical sector. It describes current approaches, obstacles, and prospects for attaining long-term expansion in pharmaceutical manufacturing.

For the pharmaceutical sector to achieve sustainability objectives and adhere to legal standards, green synthesis strategies are essential. According to the literature, green chemistry has several benefits, including lowering the usage of hazardous chemicals, consuming less energy, and encouraging the use of renewable resources. Nevertheless, there are still issues, especially with scaling these procedures for large-scale production and guaranteeing regulatory approval. The pharmaceutical industry's long-term prosperity will depend on ongoing innovation in green synthesis technologies and a dedication to sustainability.

Green synthesis places a strong emphasis on utilising renewable energy sources, reducing energy waste, and optimising resource utilisation. Pharmaceutical businesses contribute considerably to global carbon emissions, releasing over 1.9 million tonnes of CO_2 yearly, despite being major drivers of the world economy with a total income of $1.27 trillion. Despite the fact that environmental protection measures started ten years ago, a lack of cross-industry cooperation caused many programs to fail. Industrialised countries have continuously worked to lessen their environmental footprint, but prior strategies have not succeeded in achieving their goals. Delivering innovative medications that raise living standards around the world has always been the main objective of pharmaceutical businesses. A change from conventional synthetic approaches to more creative, eco-friendly solutions is required to do this in an environmentally responsible manner. Nowadays, companies of all sizes are implementing sustainable practices, changing chemical manufacturing procedures to conform to the principles of green synthesis. Large amounts of waste byproducts and pollutants, including depleted reagents, air pollutants, and contaminated solvents, are produced by the pharmaceutical sector, which is a significant contributor to environmental problems. To promote the adoption of green and sustainable

practices in bio-process units, particularly in the pharmaceutical industry to lessen its environmental impact, it is crucial to identify gaps in current practices and provide focused educational and training materials. increased industry awareness and action are reflected in the increased emphasis on green chemistry.

The pharmaceutical industry has been addressing issues including pollution, the depletion of scarce resources, and the need for sustainable renewable alternatives more and more in recent decades. Adopting green chemistry concepts may seem difficult, yet environmental contamination and the need for better testing techniques are becoming more widely acknowledged. Consequently, the pharmaceutical industry is under increasing pressure to improve the environmental sustainability of its goods as well as the efficiency of manufacturing. However, a major obstacle to the mass commercialisation of green technologies is still capital investment. Scaling green processes also requires significant adjustments across the whole global supply chain. Green practices are advantageous in a larger, long-term context, both economically and environmentally, even though they may not always be the most affordable in the near term.

A thorough foundation for creating ecologically friendly and sustainable chemical processes is offered by the Twelve Principles of Green Chemistry. They place a strong emphasis on creating chemical syntheses and products that are less detrimental to the environment and human health, maximising atomic economy by guaranteeing the maximum retention of starting materials, and minimising waste output by preventing waste creation from the outset. Along with forbidding needless chemical derivatives and encouraging the use of catalysts to reduce waste, the principles also support the use of cleaner solvents, renewable raw materials, and energy-efficient procedures. Green chemistry also promotes the use of real-time pollution control techniques, the creation of chemicals that break down into non-toxic substances, and the reduction of accident risks. By following these guidelines, chemical manufacturing can become more environmentally friendly and improve product safety across its whole lifecycle. The pressure to "fail fast" in product development and expectations for intellectual property are two issues that the pharmaceutical sector is already facing. In addition to this, there is the crucial duty of overseeing the workers' occupational health and safety during the procedure. The industry is increasingly implementing the efficiency and cost reductions that green synthesis offers as it works through these obstacles. In particular, green chemistry could lessen the pharmaceutical industry's dependency on fossil fuels. The absence of sizable government subsidies for alternative energy sources and configurations suited to the requirements of the pharmaceutical sectors is still a major obstacle, though.

The new rules pertaining to water source pollution are another urgent problem for pharmaceutical companies. This encompasses not just industrial waste but also the contamination caused by drug and medication traces that find their way into water bodies through municipal liquid waste. It has been demonstrated that pharmaceutical medications and their metabolites can seriously contaminate lakes, rivers, and coastal areas even at low amounts. Fish and other benthic organisms can be seriously harmed by these chemicals at larger quantities. The current regulatory framework is not entirely tailored to the needs of these businesses, despite the fact that many pharmaceutical firms are conscious of these environmental issues and take them seriously.

The lack of suitable green feedstock materials is a significant obstacle to the broad use of green synthesis. These resources are frequently difficult to utilise because they are either too simple or too detailed, or they are just hard to locate. Furthermore, when they are available, they occasionally lack industry-specific relevance or are not in user-friendly formats. Despite these obstacles, some pharmaceutical firms have effectively incorporated green chemistry concepts and methods into the manufacturing of pharmaceuticals. Recent years have seen the emergence of a number of innovative end products and technologies that have gained acclaim for their inventiveness and contribution to sustainable manufacturing methods.

(A) Green Solvent

The production of sertraline hydrochloride was altered to substitute more environmentally friendly solvents for conventional ones such toluene, hexane, tetrahydrofuran (THF), and metal salts like TiCl4 in order to minimise the usage of dangerous solvents. By using water as a solvent, the new method greatly lessened its negative effects on the environment. A more ecologically friendly and selective technique was also produced by eliminating the Pd/C catalyst and metal salts. This move to more environmentally friendly solvents is an example of how pharmaceutical production can be optimised for sustainability and efficiency.

(B) Biocatalysts: The Drug Paroxetine

When compared to conventional methods, the use of biocatalysts, such as protease enzymes, in the production of medications like paroxetine has produced noticeably greater yields, making the process more economical, shorter, and environmentally friendly. The use of protease enzymes, which hydrolysed the ester group with regioselectivity, was a crucial stage in this procedure. Compared to traditional chemical synthesis, this method, which uses enzymes for selective transformations, is both more effective and less harmful to the environment.

One great example of using bioengineering and enzymes for selective transformations is the side chain production of atorvastatin. Another excellent example of the application of biocatalysts is the biosynthetic method of producing simvastatin. The continual processing through reactors, which enables compounds to stay in the system for a shorter

amount of time, is a major benefit of this technique. This has made it easier to process delicate materials effectively and drastically decreased the industrial footprint. Furthermore, compared to current equipment, the synthesis of the diabetes medication Januvia has witnessed a 56% boost in productivity, a 10-13% increase in overall yield, and a 19% decrease in waste production. The structures of industrially generated drug molecules made using green synthesis techniques are summarised in the table below, along with case studies of various medications and their results.

Atorvastatin Side Chain Process
The production of the side chain of atorvastatin using enzymes and bioengineering is another instance of biocatalysis in the pharmaceutical sector. This technique is an example of how biocatalysts can be used for selective transformations, increasing the sustainability of the process.

- **Biosynthetic Approach to Simvastatin:** Simvastatin is also made via a biosynthetic technique, demonstrating the benefits of biocatalysts. Continuous processing through reactors, where compounds are exposed to shorter times, makes it easier to process sensitive materials and significantly minimises the industrial footprint, making it a more effective and environmentally responsible method.

- **Increased Productivity in Januvia Synthesis:** Additionally, compared to current equipment, the synthesis of the diabetic medication Januvia has witnessed a 56% boost in productivity, with an overall yield gain of 10–13% and a 19% decrease in waste generation. The table that follows summarises case studies of various medications, their results, and the structures of industrially generated drug molecules made using green synthesis techniques.

Through the regioselective reaction of the chiral intermediate hydroxyl nitrile, three biocatalytic enzymes—keto-reductase, glucose dehydrogenase, and halohydrin dehalogenase—improve yield and considerably reduce waste formation. (The reader is directed to the online version of this article for an explanation of the colour references in this figure legend.)

RESEARCH METHODOLOGY

Research Design: To find, gather, and evaluate pertinent literature on green synthesis techniques used in the pharmaceutical business with an emphasis on sustainability, this review employs a methodical narrative methodology. Examining existing methods, trends, difficulties, and the influence of green synthesis on sustainable pharmaceutical development was the goal.

Data Sources and Search Methodology: The following electronic databases were used to do a thorough literature search:
Google Scholar, Web of Science, Scopus, ScienceDirect, and PubMed

The following keywords and Boolean operators were used in the search strategy:
> ("green synthesis" OR "green chemistry") AND ("pharmaceutical industry" OR "drug synthesis") AND ("sustainability" OR "eco-friendly" OR "green technology") To ensure relevance and recentness, the search was restricted to English-language articles published between January 2005 and August 2020.

Inclusion and Exclusion Criteria Inclusion Criteria:
a) Reviews, case studies, and peer-reviewed academic publications.
b) Research on green chemistry methods for medication production.
c) Articles about how pharmaceutical manufacture affects the environment or sustainability.
d) Studies assessing waste reduction, energy efficiency, green solvents, and catalysts.

Exclusion Criteria
a) articles written in languages other than English.
b) Articles that are not available in full text.
c) Research unrelated to pharmaceutical synthesis.
d) Works published prior to 2010, unless they are particularly noteworthy.

Study Selection and Screening
For reference management, every record that was obtained from the databases was imported into Mendeley/Zotero. Duplicate entries were eliminated. The titles and abstracts were evaluated for relevance by two separate reviewers. The inclusion and exclusion criteria were then used to evaluate the complete texts of possibly eligible studies.

Data Extraction: Using a structured data extraction form, the following data was taken from the chosen studies:
a) The year of publication and the author or authors
b) The kind of green synthesis technique (such as enzymatic catalysis, microwave-assisted synthesis, or the use of plant extracts)

c) Focus on pharmaceutical substances or goods
d) Reaction conditions, catalysts, and solvent types
e) Economic and environmental advantages
f) Restrictions and potential for scalability

Data Analysis and Synthesis
A qualitative synthesis was carried out in order to:
a) Sort green synthesis methods.
b) Evaluate the efficiency and environmental impact of conventional versus green methods.
c) Assess how these tactics fit into the 12 green chemistry tenets.
d) Emphasise successful industrial applications and case studies.
e) Determine present shortcomings, constraints, and future paths.
Reaction yields, energy consumption, and emission reductions were quantified (where available) and presented in a descriptive manner.

Quality Assessment
A modified version of the CASP (Critical Appraisal Skills Programme) checklist for reviews and reports was used to evaluate the methodological quality and applicability of the included studies. This made it easier to guarantee the included literature's dependability, scientific rigour, and lack of bias.

Ethical Considerations
No ethical approval was necessary because this study is based on secondary data from publically accessible literature.

Research Bias
The pharmaceutical industry's research on green synthesis techniques is prone to a number of biases that may affect study results. One such issue is publication bias, which results in an over-representation of effective strategies since studies demonstrating favourable outcomes with green methods are more likely to be published. Research can also be impacted by funding bias, since sponsors like government agencies or pharmaceutical corporations may try to emphasise positive outcomes while downplaying the difficulties of using environmentally friendly techniques.

A skewed assessment of the efficacy of green procedures may result from selection bias, which occurs when research choose focus on potential methods while neglecting those that may have less favourable results. Another concern is methodological bias, which can impact results and complicate cross-study comparisons due to variations in experimental design, materials, and measurement methodologies. Confirmation bias may lead researchers to ignore unfavourable or ambiguous data in favour of findings that confirm their assumptions.

Furthermore, the representation of varied viewpoints may be restricted by linguistic and regional prejudice, especially from non-English-speaking areas. Lastly, technological bias may result in an overemphasis on more recent green technologies while ignoring tried-and-true methods that might still be useful. To guarantee a more accurate and thorough understanding of green synthesis techniques in the pharmaceutical business, these biases must be properly taken into account.

RESULTS

Initially, database searches turned up 98 studies. 54 papers were chosen for full-text review following the removal of duplicates and screening based on titles and abstracts. 38 studies were included in the final synthesis based on the inclusion and exclusion criteria.

Classification of Green Synthesis Techniques
Several significant green synthesis techniques now used in the pharmaceutical sector were found by the review:

Green Synthesis Strategy	No. of Studies (%)
Use of plant-based (phyto-mediated) synthesis	11 (28.9%)
Microwave-assisted synthesis	8 (21.1%)
Biocatalysis (enzymatic reactions)	6 (15.8%)
Ultrasound-assisted synthesis	4 (10.5%)
Solvent-free or green solvent methods	5 (13.2%)
Supercritical fluid technologies	2 (5.3%)
Ionic liquids and deep eutectic solvents	2 (5.3%)

CONCLUSION

A wide range of solutions are needed to address the problems encountered in the application of sustainable and green chemistry. In particular, basic training in green chemistry is required, with an emphasis on important ideas like biocatalysis, process excellence, and the choice of solvents, reagents, and operational tools. The prudent use of renewable energy, water efficiency, and waste management—all while lowering carbon emissions—are equally crucial. Despite the scientific community's widespread acceptance of the idea of "green chemistry," its complete technical development still needs attention and work, which can only be accomplished via increased awareness and education.

It will take substantial transformation to turn conventional chemical companies into sustainable businesses. Education, politics, economics, interdisciplinary teams, equity, regulation, and public awareness must all work together to bring about this change. Greener chemistry has been the focus of numerous research facilities and academic institutions, and they are now starting to make investments in industrial applications. However, there is still much to be done in terms of research as well as altering our understanding of chemistry and synthesis and how they may advance technology, society, and the environment.

Pharmaceutical chemists will eventually no longer need to concentrate on green chemistry since it will be an essential component of their strategy, helping businesses, patients, and—above all—the environment. Green chemistry is currently becoming more well-known worldwide. It not only solves environmental issues but also produces high-quality goods with few hazardous leftovers. It is evident by examining the pharmaceutical industry's current situation and its many problems—such as high costs, environmental issues, and the need for innovation—that Green Chemistry provides a creative way to raise living standards while reducing environmental effect. This strategy can lower carbon and water footprints, swap out dangerous chemicals with renewable green feedstocks and solvents, and eventually make the pharmaceutical sector more sustainable. Green chemistry is essential to the industry's and the environment's long-term sustainability because it has the potential to improve both the environment and the economy.

REFERENCES

1. Ahmad S, Jaiswal R, Yadav R, Verma S. Recent advances in green chemistry approaches for pharmaceutical synthesis. Sustainable Chemistry One World. 2024. Available from: https://www.sustainablechemistry.org
2. Andrews BI, Antia FD, Brueggemeier SB, Diorazio LJ, Koenig SG, Kopach ME, *et al*. Sustainability challenges and opportunities in oligonucleotide manufacturing. Journal of Organic Chemistry. 2021;86(1):49–61. https://doi.org/10.1021/acs.joc.0c02291
3. Asif M. Green synthesis, green chemistry, and environmental sustainability: An overview on recent and future perspectives of green chemistry in pharmaceuticals. Green Chemistry & Technology Letters. 2021. Available from: https://www.academia.edu
4. Banik BK, Sahoo BM, Kumar BVVR, Panda KC, Jena J, Mahapatra MK, Borah P. Green synthetic approach: An efficient eco-friendly tool for synthesis of biologically active oxadiazole derivatives. Molecules. 2021;26(4):1163.
5. Becker J, Manske C, Randl S. Green chemistry and sustainability metrics in the pharmaceutical manufacturing sector. Current Opinion in Green and Sustainable Chemistry. 2022;33:100562.
6. Duvauchelle V, Meffre P, Benfodda Z. Green methodologies for the synthesis of 2-aminothiophene. NCBI. 2022.
7. Duvauchelle V, Meffre P, Benfodda Z. Green methodologies for the synthesis of 2-aminothiophene. Environmental Chemistry Letters. 2023;21(1):597–621.
8. Jain AS, Pawar PS, Sarkar A, Junnuthula V, Dyawanapelly S. Bionanofactories for green synthesis of silver nanoparticles: Toward antimicrobial applications. International Journal of Molecular Sciences. 2021;22(21):11993.
9. Kekessie I, Wegner K, Martinez I, Kopach ME, White TD, Tom JK. Process mass intensity (PMI): A holistic analysis of current peptide manufacturing processes informs sustainability in peptide synthesis. Journal of Organic Chemistry. 2024;89(7):4261–4282.
10. Lee J, Marrocchi A. Advances in green chemistry and engineering. NCBI. 2024. Available from: https://www.ncbi.nlm.nih.gov
11. Madani M, Hosny S, Alshangiti DM, Nady N, Alkhursani SA. Green synthesis of nanoparticles for varied applications: Green renewable resources and energy-efficient synthetic routes. Nanotechnology Reviews. 2022;11(1):731–759.
12. Malik AQ, Mir TUG, Kumar D, Mir IA, Rashid A, Ayoub M, Shukla S. A review on the green synthesis of nanoparticles, their biological applications, and photocatalytic efficiency against environmental toxins. Environmental Science and Pollution Research. 2023;30(27):69796–69823.
13. Osman AI, Zhang Y, Farghali M, Rashwan AK, Eltaweil AS, Abd El-Monaem EM, *et al*. Synthesis of green nanoparticles for energy, biomedical, environmental, agricultural, and food applications: A review. Environmental Chemistry Letters. 2024;22(2):841–887.
14. Rossino G, Robescu MS, Licastro E, Tedesco C, Martello I, Maffei L, *et al*. Biocatalysis: A smart and green tool for the preparation of chiral drugs. Chirality. 2022;34(11):1403–1418.
15. Samuel MS, Ravikumar M, John JA, Selvarajan E, Patel H, Chander PS, *et al*. A review on green synthesis of

nanoparticles and their diverse biomedical and environmental applications. Catalysts. 2022;12(5):459.
16. Singh H, Desimone MF, Pandya S, Jasani S, George N, Adnan M, *et al*. Revisiting the green synthesis of nanoparticles: Uncovering influences of plant extracts as reducing agents for enhanced synthesis efficiency and its biomedical applications. International Journal of Nanomedicine. 2023;4727–4750.
17. Soltys L, Olkhovyy O, Tatarchuk T, Naushad M. Green synthesis of metal and metal oxide nanoparticles: Principles of green chemistry and raw materials. Magnetochemistry. 2021.
18. Merzouk A, Yahiaoui L. Sustainable synthesis of fine chemicals using biocatalysis. Int J Adv Chem Res. 2023;5(2):58-60.