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Review Article

Green chemistry principles in the pharmaceutical industry: a way toward sustainable drug development

Doaa A. Habib[1]*, Sarah H. Elewa[1]

[1]Department of Pharmaceutical Technology, Faculty of Pharmacy, Alsalam University in Egypt

*Corresponding author: Doaa A. Habib:

E-mail address: doaa.habib@sue.edu.eg

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Abstract

Green chemistry has increasingly become an essential paradigm in pharmaceutical research and production, meeting the growing demands of regulations and the environment. Green chemistry, which emphasizes concepts like waste reduction, atom economy, and the use of safer reaction conditions, makes it easier to create effective and sustainable methods for drug discovery and production. Green chemistry offers a range of environmentally benign approaches for the synthesis of pharmaceutical compounds, aiming to minimize hazardous waste, energy consumption, and the use of toxic reagents during drug development. Such approaches include multicomponent reactions (MCRs) and various catalytic strategies (homogeneous, heterogeneous, and single-atom catalysis). Green chemistry was applied in the pharmaceutical industry; for example, its principles are used in nanoparticle formulations, biocatalysis, and cosmetics. By enabling the manufacture of nanoparticles using environmentally friendly techniques that reduce the use of hazardous chemicals and waste production, the incorporation of green chemistry principles into pharmaceutical nanotechnology has completely transformed drug delivery systems. In addition to improving the therapeutic efficacy and biocompatibility of nanocarriers, this sustainable technique complies with legal requirements for ecologically conscious production. Similar to this, using biocatalysis in green chemistry frameworks reduces the need for harsh reaction conditions and hazardous chemicals by providing a benign, energy-efficient, and selective reaction environment for the synthesis of complex pharmaceutical intermediates and active ingredients. By promoting the use of renewable, biodegradable raw ingredients and green solvents, green chemistry simultaneously promotes innovation in cosmetic formulations while enhancing product safety and environmental effect. When taken as a whole, these developments highlight how important green chemistry is to changing the pharmaceutical and cosmetics sectors toward high-performance, affordable, and sustainable solutions.

Keywords: Green chemistry, multicomponent reactions, catalysis, nanoparticles, cosmetics, pharmaceutical Manufacturing.

Introduction

Green synthesis seeks to enhance resource efficiency, minimize energy waste, and utilize renewable energy sources for power generation. Although pharmaceutical companies are significant contributors to the global economy, they are also a primary source of carbon emissions, producing approximately 1.9 Mt CO_2 (Dhasmana et al., 2018). Although the concept of environmental preservation was initiated a decade ago, numerous implementations faltered due to insufficient collaboration across companies (Singh & Pandey, 2019). Every pharmaceutical company has always aimed to provide innovative medications that will raise people's quality of life everywhere. Drug development procedures that incorporate green chemistry guarantee that these advancements are not only efficient but also environmentally sustainable. Green chemistry concepts reduce the environmental impact of pharmaceutical manufacture while encouraging safer, more economical production by reducing waste and harmful reagents (Anastas & Warner, 1998). By facilitating scalable, environmentally responsible solutions that satisfy both therapeutic needs and environmental obligations, this alignment advances sustainable healthcare breakthroughs globally and advances global health goals (Sheldon, 2016). Accordingly, companies must move from classic synthetic techniques to a modern inventive mechanism to achieve this goal in an environmentally friendly manner. Large companies and small companies alike have already taken steps to adapt in a sustainable manner by changing chemical manufacturing procedures to produce products using green chemistry concepts

(Clark & Macquarrie, 2002).The terms "green chemistry," "clean chemistry," and "benign chemistry" refer to methods that reduce the amount of energy and reagents used, feedstocks used, and waste produced in the chemical and analytical industries in order to preserve resources and the environment (Bandichhor, 2018). As a result, several alternatives and plans have been presented, and there is a high level of awareness regarding greening the available analytical procedures. Reagent reduction, solvent depletion, waste minimization and recycling, and the passivation and degradation of toxic wastes are the foundations of this. Eliminating hazardous substances by substituting them with safer ones is another goal of such practices (De la Guardia & Ruzicka, 1995).Green chemistry is vital in pharmaceutical manufacturing since it fosters safer, more sustainable, and economically efficient medication development procedures. By reducing the utilization of poisonous reagents and hazardous solvents, green chemistry mitigates environmental pollution and improves the safety of workers and patients (Ratia, 2023). The adoption of biocatalytic methods and solvent recycling might markedly diminish waste and energy usage in pharmaceutical production. These advancements not only advantage the environment but also augment the economic and therapeutic value of pharmaceuticals (Kumar & Sharma, 2020).

Preparation of drugs by using green chemistry approaches Design and settings

Multicomponent reactions (MCRs)

Multicomponent reactions (MCRs) have become a potent approach in synthetic organic chemistry owing to their extensive applications in drug discovery and development. Flexible transformations of MCRs occur when three or more substrates react to create very atomically efficient, structurally complex products. The medicinal chemistry community is beginning to see MCRs as a very exploratory and evolutionary technique that can lead to the synthesis of physiologically active compounds in a quicker, more economical, and more sustainable manner. Drug development has adopted substantial use of MCR-based synthetic approaches in recent years, and MCRs have been used to synthesize a number of anticancer medications (Zhang & Smith, 2023). The utilization of multicomponent reactions (MCRs), especially in aqueous or solvent-free environments, to create complex drug-like compounds in a single step is a very sustainable approach in pharmaceutical synthesis. By combining nearly all reactants into the final product and reducing by-products, these MCRs significantly improve atom economy. Three or more starting ingredients, such as amines, aldehydes, isocyanides, or carboxylic acids, react in a single-pot operation, as presented in Figure (1). Because fewer intermediate isolation processes are required, this method simplifies purification while using less solvent and producing less waste. The reaction may be gradually scaled when coupled with continuous-flow processing, which enhances heat and mass transfer, allows for exact control of reaction parameters, and makes active pharmaceutical ingredient (API) production quicker, safer, and more environmentally friendly. The end effect is a pharmaceutical manufacturing process that is quicker, less wasteful, more energy-efficient, and safe for the environment (Zhang et al., 2020).

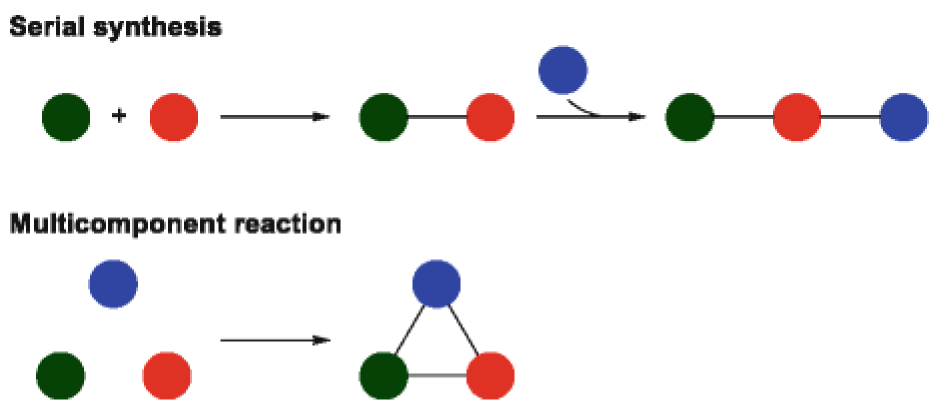

Figure 1: Multicomponent reaction

Catalysis approach in green chemistry

A key strategy in green chemistry is catalysis, which improves selectivity, reduces waste, and lowers energy requirements to increase the sustainability and efficiency of chemical processes. Catalysis reduces the environmental effect of pharmaceutical manufacturing by enabling reactions to continue at softer conditions with higher yields and fewer by-products. Stoichiometric reagents can be substituted with a catalytic method, which improves atom economy and reduces hazardous waste. Catalysis is an essential tool for environmentally friendly pharmaceutical manufacture because it may be used to drive a diversity of reactions that are essential for drug development using both biological and chemical catalysts (Graziano et al., 2023). The two main categories of catalysts used in green chemistry are homogeneous and heterogeneous. Particularly in asymmetric synthesis, homogeneous catalysts, which are in the same phase as the reactants and are usually dissolved in a solvent, enable superior molecular-level interaction along with high selectivity. Unfortunately, it can be difficult to separate them from the product combination. Heterogeneous catalysts, on the other hand, are in a distinct phase. For example, solid catalysts can interact with liquid or gas reactants to make separation and catalyst reuse simple, which is beneficial for industrial scaling. The two types make distinct contributions to environmentally friendly drug production; heterogeneous catalysts are chosen for their ease of recovery and environmental advantages, while homogeneous catalysts are selected for precision reactions (Sheldon, 2019). Single-atom catalysts (SACs) have emerged as a distinct and innovative class of catalytic materials that combine the molecular-level precision of homogeneous catalysts with the recoverability and stability of heterogeneous systems. These catalysts consist of isolated metal atoms dispersed on solid supports, enabling near-complete atom utilization and significantly reducing the generation of chemical waste. In the context of green chemistry, SACs align closely with key principles such as improved atom economy, reduced hazardous byproducts, and energy- efficient processes. Their application in pharmaceutical synthesis particularly in cross-coupling, hydrogenation, and multicomponent reactions, has demonstrated high selectivity, operational simplicity, and compatibility with continuous-flow and one-pot systems. Thus, SACs represent a strategic advancement in sustainable drug development, offering a balanced solution between catalytic performance and environmental impact (Dua et al., 2020). For instance, Pt1/FeOx has shown remarkable catalytic activity for CO oxidation, achieving high turnover frequencies (TOFs) under mild conditions while minimizing precious metal usage. Such systems offer promising avenues for sustainable catalytic design by maximizing reactivity per metal atom and enhancing selectivity (Qiao et al., 2011).

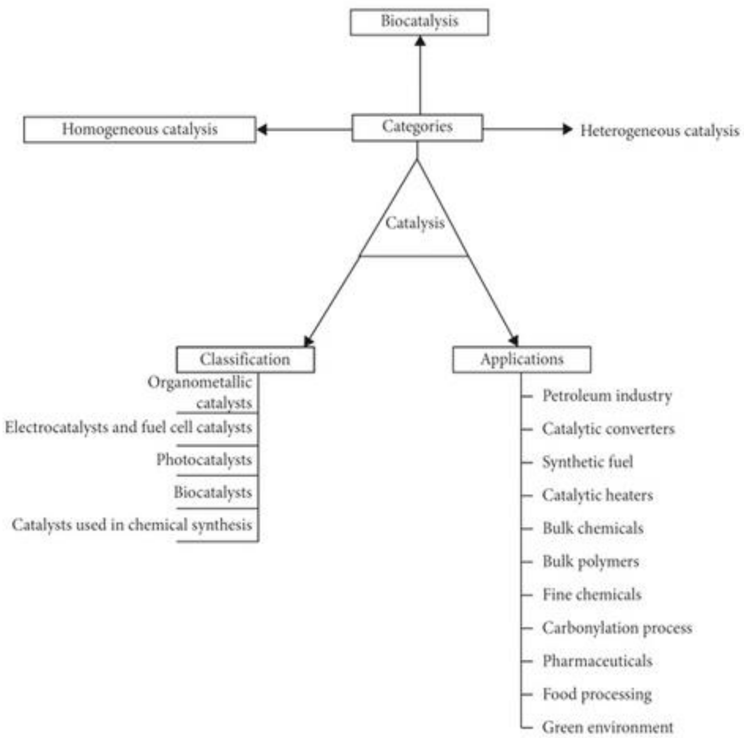

Figure (2) :shows the categories, classification, and applications of catalysis used in green chemistry (Odularu, 2020).

The principles of green chemistry in pharmaceutical drug development

It is now strategically necessary to include the 12 principles of green chemistry in pharmaceutical development to meet regulatory requirements, cost-effectiveness, and enhanced environmental performance. These principles, for instance, atom economy, guide chemists in creating synthetic pathways that are less dangerous and more sustainable by the use of safer solvents, catalysis, energy efficiency, and design for degradation. Chemists are guided in creating synthetic pathways that are less dangerous and more sustainable by the use of safer solvents, catalysis, energy efficiency, and design for degradation. To reduce waste and resource consumption, measures such as the Process Mass Intensity (PMI) and E-factor are being used more and more in process design. Early use of green chemistry in the synthesis of active pharmaceutical ingredients (APIs) promotes sustainability objectives while simultaneously increasing process effectiveness and product safety. Recent studies support a "benign by design" strategy in which human safety, medicinal efficacy, and environmental impact are all taken into taken into account simultaneously while developing new drugs (Madani et al., 2022). In order to integrate environmental safety into drug design, recent developments in green pharmaceutical science have put forth frameworks such as GREENER (green and environmental evaluation for novel emerging responsible pharmaceuticals). To make sure that pharmaceutical chemicals are efficient, biodegradable, and present few ecological hazards, this method promotes interdisciplinary cooperation between synthetic chemists, toxicologists, and environmental scientists. Waste and energy consumption in the synthesis of drug candidates are being decreased by employing techniques including biocatalysis, mechanochemical synthesis, and the use of renewable solvents. Furthermore, the One Health model emphasizes the necessity of evaluating APIs during their whole life cycle, especially to prevent their build-up in aquatic systems, the emergence of antibiotic resistance, or unanticipated adverse effects. Regulatory advice and sustainability reporting throughout pharmaceutical pipelines are currently informed by this integrated model (Sheldon, 2023). The 12 principles of green chemistry are presented in Figure (3) (Boxall et al., 2023).

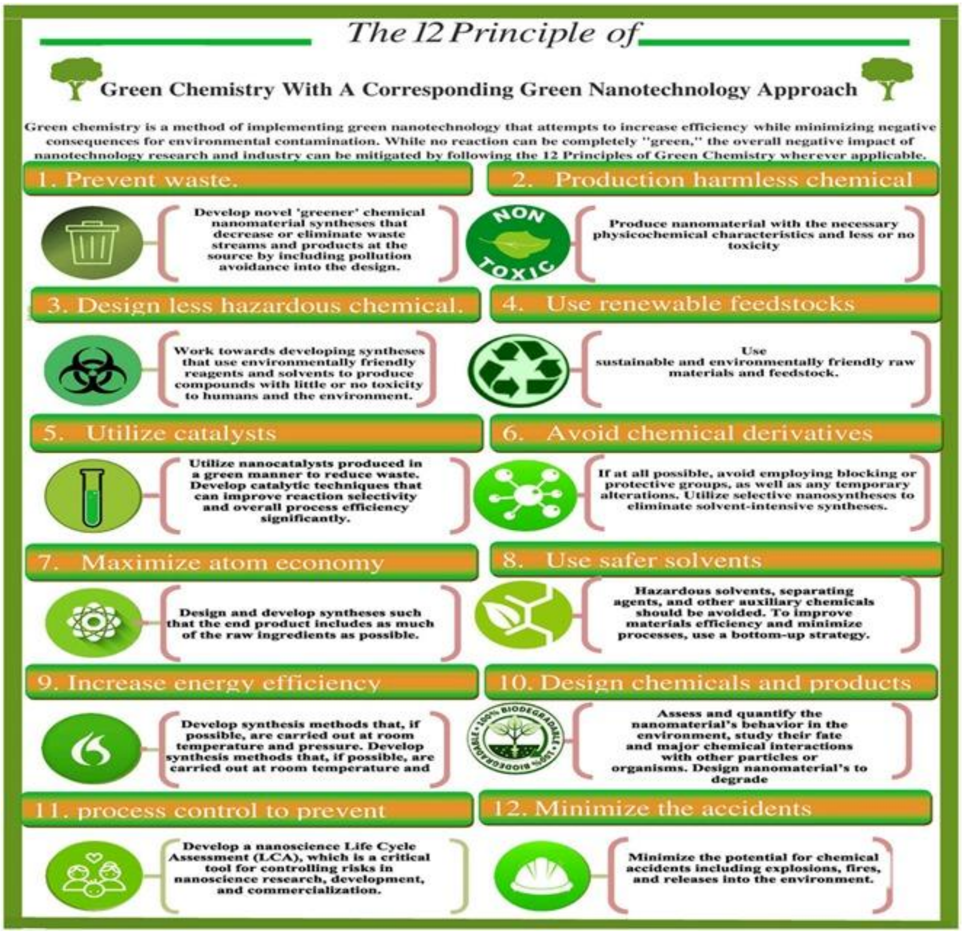

Figure 3: Green chemistry principles

The applications of green chemistry in the pharmaceutical industry

The use of green chemistry in nanoparticles formulations

The utilization of green chemistry in nanoparticle synthesis for drug delivery has surfaced as a sustainable and friendly alternative to traditional chemical approaches. This environmentally sustainable method employs natural reducing and stabilizing agents, such as plant extracts, microbes, or biopolymers, thus obviating the necessity for hazardous chemicals and energy-intensive processes (Ovais et al., 2017). Nanoparticles formulated by using environmentally friendly methods frequently demonstrate improved biocompatibility, stability, and targeted drug delivery capabilities, rendering them optimal for biomedical applications, especially in oncology. Recent research has shown that green-synthesized nanoparticles, including silver and gold nanoparticles, exhibit promising anticancer, antibacterial, and anti-inflammatory activities with little cytotoxicity to healthy tissues. These particles can be designed to increase pharmacokinetics, bioavailability, and cellular uptake of active pharmaceutical ingredients (Soliman & El-Kazzaz, 2024). For an instance of how green chemistry can enable scalable, environmentally friendly nanotherapeutics that could be developed into topical or systemic antimicrobial formulations, there is the synthesis of silver nanoparticles (AgNPs) using Curcuma longa (turmeric) flower extract. This process produces monodisperse spherical AgNPs (5-25 nm) with strong antibacterial activity against Staphylococcus aureus, Klebsiella pneumoniae, and Mycobacterium species, while exhibiting minimal cytotoxicity on healthy tissues (Bharadwaj et al., 2021). Green chemistry-enabled synthesis of gold nanoparticles using Cannabis sativa extract, followed by doxorubicin loading, resulted in a significant enhancement of anticancer activity. The formulation exhibited strong therapeutic efficacy in lung cancer models, demonstrating improved drug delivery and cellular uptake. These findings highlight the potential of eco-friendly nanocarriers in advancing targeted cancer therapies (Smith & Lee, 2022). Green synthesis of antiviral nanoparticles is emerging as a sustainable and effective approach in nanomedicines. Recent studies in Egypt have demonstrated that silver and zinc oxide nanoparticles synthesized using plant extracts can inhibit respiratory and herpes viruses. These eco-friendly nanoparticles offer antiviral activity with improved safety profiles, supporting their potential use in future therapeutic formulations. The green chemistry approach eliminates toxic reagents and aligns with global trends in sustainable pharmaceutical development (Is et al., 2022).

Utilizing Green Solvents for Biocatalysis in Pharmaceutical industry

The use of biocatalysts in environmentally friendly solvents, like deep eutectic solvents (DESs), is increasing in appeal in the pharmaceutical industry because of their capacity to promote specific chemical reactions in safe and mild environments. DESs, which are frequently made of choline chloride mixed with other hydrogen bond donors, "offer a promising green medium for biocatalysis, enhancing enzyme stability, activity, and selectivity, according to Xu et al. (2017). Additionally, they highlighted that "lipase-catalyzed reactions performed in choline chloride-based DESs showed improved enantioselectivity and higher yields compared to traditional organic solvents," which is in line with the fundamentals of green chemistry by lowering the use of hazardous chemicals and the production of waste. These results highlight how DESs can support environmentally friendly pharmaceutical operations by taking the place of hazardous solvents(Albulaihed et al., 2024). Recent investigations have demonstrated that deep eutectic solvents (DESs) substantially enhance enzymatic performance by improving both activity and stability. For instance, Yadav and Venkatesu (2022) reviewed how DESs enable protein stabilization, refolding, and activation, in some cases increasing enzymatic activity several-fold Furthermore, a 2023 study revealed that the incorporation of DESs as co-solvents increased the catalytic efficiency of a transaminase enzyme (ω-TA) by up to 2.4-fold and enhanced thermal stability by 2.7-fold compared to conventional buffer systems. Deep eutectic solvents (DESs) have recently emerged as environmentally friendly media that enhance enzymatic reactions by improving enzyme stability and catalytic efficiency. Their unique physicochemical properties, such as low toxicity, biodegradability, and tunable polarity, contribute to creating favorable microenvironments for biocatalysts. Recent pharmaceutical studies demonstrate that DESs facilitate enhanced enzymatic transformations in drug synthesis, improving yields and reducing reaction times. These solvents offer a sustainable alternative to conventional organic solvents, aligning with green chemistry principles and advancing biocatalysis applications in pharmaceutical manufacturing (Rathee et al., 2023).

The use of green chemistry principles in cosmetic preparations

The use of green chemistry has become essential in pharmaceutical manufacturing facilities that also make cosmeceutical formulations in order to provide safe, sustainable, and environmentally friendly cosmetics. In order to effectively extract and stabilize bioactive plant compounds, such as phenolics, flavonoids, and terpenes, used in creams, serums, and lotions, one important tactic is to substitute green solvents, such as natural deep eutectic solvents (NaDES) and biomass-derived solvents, for conventional organic solvents (Xu et al., 2017). A number of green chemistry principles are also followed by the development and application of bio-based surfactants, such as sucrose esters and alkyl polyglucosides (APGs), which allow for gentle, biodegradable, and biocompatible emulsification in personal care products instead of harsher petrochemical surfactants. When taken as a whole, these developments promote decreased toxicity, improved biodegradability, and less environmental effect, meeting needs for safer cosmetic components and environmentally friendly production methods in the pharmaceutical and cosmetics sectors worldwide (Wawoczny & Gillner, 2023). Recent advances in green cosmetic formulations are incorporating enzymatic processing and plant-based preservatives to broaden scope and efficacy. For example, hydrolyzed plant proteins and peptides obtained via enzymatic hydrolysis (soy, wheat, and rice) are used as bioactive ingredients to deliver antioxidant, anti-inflammatory, and anti-aging effects in skincare formulations. Plant phenolic molecules have been proposed as natural preservatives replacing synthetic ones due to their antimicrobial properties and lower toxicity. These strategies increase product safety and sustainability, aligning cosmetic science with green chemistry by reducing reliance on harmful chemicals and exploiting renewable biological resources (Stubbs et al., 2022).

Future Aspects in the Application of Green Chemistry Principles in Pharmaceutical Manufacturing

In light of growing environmental concerns and regulatory pressures, the future of green chemistry in pharmaceutical manufacturing is poised to focus on technological innovation, adoption of continuous flow processing, and predictive process optimization. Process intensification innovations, including continuous-flow reactors, photochemical synthesis, and electrochemical synthesis, provide approaches to cut waste and energy use while enhancing safety and scalability in the manufacturing of APIs (Wen et al., 2023). Moreover, applying green chemistry principles early in drug discovery allows for designing APIs with enhanced atom economy, reduced step count, and minimal hazardous byproducts, facilitating more eco-efficient scaled manufacturing (Pollard & Woodley, 2007). Emerging tools like real-time monitoring and machine-learning models, driven by predictive simulations, are expected to play key roles in optimizing reaction conditions, predicting yields, and reducing resource input, all aligned with sustainable production trends (Kar et al., 2022). Finally, aligning green chemistry implementation with regulatory incentives, interdisciplinary collaboration, and stakeholder engagement will be crucial to drive cost-effective and industrial-scale transitions toward carbon-neutral, resource-efficient pharmaceutical processes. AI and machine learning are increasingly used in green chemistry to optimize reaction conditions, reduce waste, and improve process control. Recent studies show that AI can predict green solvent properties, guide enzyme-based reactions, and enable real-time process adjustments, all contributing to more sustainable pharmaceutical manufacturing (Ferreira & Sarraguça, 2024).

Conclusion

In conclusion, incorporating green chemistry concepts into the production of pharmaceuticals and cosmetics is a critical step in the direction of developing products that are socially conscious, commercially feasible, and environmentally sustainable. The ecological effect of these sectors has been greatly diminished by the implementation of fundamental green chemistry techniques, such as waste minimization, atom economy, cleaner solvents, and energy efficiency. Applications of green chemistry principles in nanotechnology and biocatalysis illustrate how scientific innovation can directly support sustainability goals. While nanocarriers in cosmetics improve skin penetration and stability of active ingredients, nanoparticles in medicines provide superior drug delivery with better targeting and fewer adverse reactions. On the flip side, biocatalysis makes it possible for highly selective, mild-condition synthesis, which lessens the requirement for dangerous reagents in formulations for both medications and cosmetics. Additionally, the potential for more environmentally friendly extraction, formulation, and preservation has increased with the introduction of bio-based surfactants and natural deep eutectic solvents (NaDES) in creams, lotions, and serums. As regulatory frameworks and consumer expectations increasingly favour green and clean-label products, both the pharmaceutical and cosmetic sectors must continue investing in sustainable technologies from the earliest design stages to large-scale production. Future efforts should prioritize scaling up these innovations, improving cost-efficiency, and fostering interdisciplinary collaboration to fully realize the potential of green chemistry.

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