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Review Article

GREEN AND SUSTAINABLE APPROACHES TO THE DESIGN OF MANUFACTURE OF MEDICINAL AGENTS

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ABSTRACT

The Pharmaceutical Framework for Europe considers the environmental repercussions at every stage in the life span of therapeutic agents, from molecular conception and industrial fabrication through clinical utilization to waste management. During the last decade, the discipline of green and sustainable chemistry has significantly reshaped drug sciences by advancing ecological responsibility and minimizing ecological hazards. This article surveys the contemporary innovations in environmentally benign strategies utilized in medicinal design and chemical production, encompassing fundamental concepts, pioneering tools, and progressive methodologies. Drawing upon the examination of over 80 academic publications, it illustrates the practical incorporation of sustainable chemistry codes into pharmaceutical pipelines, highlighting verified successes and the ecological gains obtained. Consequently, this review emphasizes the constructive transformations driven by eco-conscious chemistry in drug manufacture and stresses the necessity for further exploration into the creation and large-scale preparation of more environmentally sound entities, in addition to advancing measures for contamination control and remediation.

Keywords: Sustainable chemistry, Eco-friendly drug discovery, Medicinal agent synthesis, Environmentally benign approaches in pharmaceuticals

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INTRODUCTION

The European industrial sector continues to generate and utilize large volumes of hazardous chemicals, many of which are eventually released into the environment, posing potential risks to public health. At the same time, Europe upholds some of the world's strictest chemical regulations and most ambitious environmental initiatives, exemplified by the EU Chemicals Strategy [1] and the Zero Pollution Action Plan [2]. Industrial compounds are primarily regulated under the REACH framework [3], while additional legislations govern specific categories such as biocides, pesticides, cosmetics, and pharmaceuticals [4].

The European Pharmaceutical Strategy aims to strengthen the sector by promoting research and innovation that address patient needs, while simultaneously addressing market failures. This strategy complements the European Green Deal, particularly the Zero Pollution agenda, which emphasizes minimizing the environmental footprint of medicinal products. It is also aligned with the EU's climate neutrality target, emphasizing reductions in greenhouse gas emissions across the pharmaceutical supply chain. Moreover, the strategy supports wider European initiatives, including the European Pillar of Social Rights, the Union of Equality, the European digital agenda, the health data space initiative, the One Health Action Plan on antimicrobial resistance, and the new European industrial strategy.

The manufacture, utilization, and disposal of pharmaceutical products create notable environmental challenges, as residues and waste can enter ecosystems. These contaminants may include substances with endocrine-disrupting properties or compounds that increase the risk of antimicrobial resistance. The presence of antibiotics in water and soil can accelerate the emergence of resistant microorganisms. To mitigate these risks, interventions must be applied throughout the entire life cycle of pharmaceuticals, ensuring efficient use of resources, reduced emissions, and minimal release of pharmaceutical residues into the environment. Unused or expired medications also represent a considerable source of waste, compounding the ecological burden. Recently, the European Commission introduced new regulations for the separate collection of household hazardous waste, which explicitly includes pharmaceuticals [5]. Additional measures to curb waste generation should also be explored. The pharmaceutical industry must be guided by innovation, implementing sustainable and climate-neutral approaches in drug design and production, and adopting the best available technologies to limit emissions and support the EU's broader climate commitments.

Within this context, green chemistry has gained increasing attention in scientific and industrial domains due to its potential to foster chemical innovation while meeting both economic and environmental goals. Emerging in the early 1990s through the work of Paul Anastas and John Warner [6], green chemistry was defined as the "design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances" [7]. Often referred to as sustainable chemistry, this discipline emphasizes methods that reduce pollution, conserve non-renewable resources, and enable cost-effective, efficient processes [8].

The concept was initially motivated by escalating environmental pollution, much of which stemmed from the chemical sector. To counter these issues, Anastas and Warner proposed the 12 Codes of Green Chemistry in 1998, offering a framework to make chemical synthesis safer for humans and ecosystems. Rather than being a separate sub-discipline, green chemistry serves as a guiding framework—a set of practices aimed at reducing the ecological footprint of chemical activities across all stages of a product's life cycle, from molecular design to end-of-life disposal.

Today, the scope of green chemistry has expanded dramatically, influencing a variety of industries including aerospace, automotive, cosmetics, electronics, energy, agriculture, household products, and pharmaceuticals [9]. Importantly, pharmaceutical manufacturing is known to produce some of the highest E-factors (a metric introduced by Roger Sheldon [10]), often ranging from 25 to 100+, highlighting the urgency of implementing sustainable practices in drug development. For every kilogram of an active pharmaceutical ingredient (Active Pharmaceutical Ingredient (API)) manufactured, approximately 25 to 67 kilograms of waste may be generated. This large amount of by-product is primarily attributed to the heavy

reliance on organic solvents, which constitute 80–90% of the total mass employed during the synthesis of fine chemicals and pharmaceutical products [11].

MATERIALS AND METHODS

A systematic review methodology was adopted to gather academic literature pertinent to green chemistry practices and sustainable synthesis pathways. More than 80 peer-reviewed articles published between 2000 and 2024 were analyzed, covering both the early milestones of the field and more recent advancements. In a few cases, earlier influential works were also considered due to their enduring significance. This timeframe reflects major progress following the formulation of the 12 Codes of Green Chemistry and the growing global focus on sustainable chemical production.

The literature search was carried out using major academic databases, including Scopus, Web of Science, PubMed, and ScienceDirect. These platforms were chosen for their comprehensive coverage of environmental sciences, chemical engineering, and multidisciplinary sustainability research. A diverse range of keywords was applied, such as "sustainable synthesis," "green solvents," "atom economy," "catalytic atom efficiency," "renewable feedstocks," and "bio-based chemicals." Boolean logic, truncation, and phrase searching were used to maximize retrieval and ensure inclusion of terminology variations.

A two-phase screening protocol was implemented. Initially, titles and abstracts were screened for relevance; subsequently, full-text assessments were performed to verify eligibility based on the selection criteria.

Inclusion criteria required studies to be: (i) published in English, (ii) peer-reviewed, and (iii) directly related to green or sustainable pharmaceutical synthesis. Publications that only briefly referenced sustainability or focused exclusively on traditional synthetic methodologies without considering environmental dimensions were excluded.

The review ultimately highlighted both the progress achieved and the persistent challenges in sustainable chemistry, establishing a solid foundation for ongoing investigation and practical implementation.

The codes of green chemistry

In 1998, the concept of green synthetic design was formally articulated by Paul Anastas (U. S. Environmental Protection Agency) and John Warner (Warner Babcock Institute for Green Chemistry). They proposed what became known as the 12 Codes of Green Chemistry, a comprehensive framework intended to guide the creation of safer and more sustainable chemical processes and products [12].

These codes address the entire life cycle of chemical activity, from the selection of raw feedstocks to the environmental fate of final products, including their toxicity, degradability, and efficiency. Over the years, they have remained the cornerstone for sustainable process design, ensuring that future innovations reduce hazards while optimizing resource use.

The 12 codes (table 1, 2) outline essential criteria that modern chemical processes and newly developed products must strive to achieve.

Table 1: The summary of the codes of green chemistry

Code	Description
Code 1. Waste Avoidance	Preventing waste at the source is better than managing or cleaning it afterward [3]
Code 2. Material Efficiency	Chemical methods should ensure that most, if not all, of the input materials are incorporated into the final product [3]
Code 3. Low-Toxicity Routes	Whenever possible, synthetic methods should use and generate substances with little or no harm to humans or the environment [3]
Code 4. Safer Molecular Design	Products should be engineered to perform their function while being as non-toxic as possible [3]
Code 5. Green Solvents	The use of auxiliary substances such as solvents or separation agents should be minimized or replaced with safer options [3]
Code 6. Energy Optimization	Processes should be designed to consume less energy, ideally operating at room temperature and pressure [3]
Code 7. Renewable Sources	Raw materials should come from renewable feedstocks whenever it is technically and economically feasible [3]
Code 8. Minimize Derivatives	Unnecessary steps such as blocking, protecting, or modifying groups should be avoided to simplify synthesis [3]
Code 9. Catalytic Preference	Catalytic processes are preferred over stoichiometric ones because they are more efficient and selective [3]
Code 10. Degradable Design	Substances should be created to break down into safe, non-persistent by-products after use [3]
Code 11. Real-Time Analysis	Analytical techniques should enable continuous monitoring to prevent pollution and improve control [3]
Code 12. Inherent Safety	Chemical processes should be designed to minimize risks of accidents such as leaks, explosions, or fires [3]

Green chemistry strategies in pharmaceutical synthesis

Green chemistry strategies play a crucial role in pharmaceutical manufacturing as they lower production expenses, improve energy utilization, and ensure that processes remain environmentally sustainable.

Microwave-assisted method

Microwave-assisted synthesis is an emerging, cost-effective, and energy-saving technique that is gaining increasing attention in pharmaceutical applications [26]. By employing microwave radiation as an alternative energy input, numerous organic reactions can be completed within minutes rather than hours or days.

Microwave heating works by converting electromagnetic radiation into thermal energy through the interaction of molecules with alternating electric fields. The wavelength of this radiation ranges from 0.001 to 1 m, with frequencies between 0.3 and 300 GHz. Heat generation occurs primarily through two mechanisms: ionic conduction and dipolar polarization [27–29].

The success of microwave-based drug synthesis largely depends on the reaction medium's ability to absorb microwave energy and the choice of solvent system used in the process [30]. In organic synthesis, polar solvents such as DMF, DMA, DMSO, N-Methyl-2-pyrrolidone (NMP), methanol, ethanol, and acetic acid are favored due to their polarity. Additionally, solvents with higher boiling points are desirable since they can significantly

accelerate reaction rates [31]. In contrast, nonpolar solvents like toluene, dioxane, and THF are generally ineffective unless other components in the mixture can interact with microwave radiation, as nonpolar molecules do not efficiently absorb microwave energy [32].

Table 2: Full description, application, and study illustration of green chemistry codes

Code	Core Idea	Explanation	Pharma Application	Study Illustration
Code 1. Waste Avoidance	Prevention	Stopping waste generation is better than treating or cleaning it later.	Real-time monitoring to optimize synthesis, cut waste, and maintain quality.	Bekker *et al.* showed ~40% of unused/expired medicines in the Netherlands could be avoided [13].
Code 2. Material Efficiency	Atom Economy	Chemical routes should maximize incorporation of starting reagents into the product.	Designing synthetic methods with minimal by-products and maximum yield.	Reactions with ≥59% yield are excellent; ≤20% yield is considered poor [14].
Code 3. Low-Toxicity Routes	Safer Synthesis	Reactions should employ and produce compounds with little or no toxicity.	Avoiding protective groups and unnecessary steps to streamline production.	Continuous-flow ibuprofen synthesis using trifluorosulfonic acid avoids extra derivatization [15].
Code 4. Safer Molecular Design	Designing Safer Chemicals	Drugs and intermediates should retain function while minimizing toxicity.	Choosing molecules with reduced hazard and eco-friendly degradation.	Example: polylactic acid (PLA) polymers from renewable sources, biodegradable after use [16].
Code 5. Green Solvents	Safer Solvents and Auxiliaries	Minimize or replace harmful solvents and auxiliaries whenever possible.	Using water or benign alternatives in place of hazardous solvents.	Solvent-free diphenylmethane (DPM) synthesis demonstrates this approach [17].
Code 6. Energy Optimization	Energy Efficiency	Reactions should minimize energy demand; ideally run at ambient conditions.	Adopting microwave/ultrasound-assisted synthesis to save energy.	Mitsunobu reaction retains efficiency even at room temperature [18].
Code 7. Renewable Sources	Use of Renewable Feedstocks	Prefer renewable inputs over non-renewable whenever feasible.	Incorporating biomass-derived or sustainable raw materials in drug design.	Enzymatic esterification of ibuprofen using glycerol; paracetamol synthesis from renewable phenol feedstock [19, 20].
Code 8. Minimize Derivatives	Reduce Derivatization	Unnecessary derivatization steps (protection/deprotection) should be avoided.	Simplify synthesis by designing direct routes to active compounds.	Green synthesis of certain antibiotics without protecting groups demonstrates efficiency.
Code 9. Catalytic Preference	Catalysis	Catalytic reagents are superior to stoichiometric ones for efficiency and selectivity.	Using enzyme or metal catalysts instead of excess reagents.	Lipase-catalyzed resolution of racemic drugs like ibuprofen shows efficiency with less waste.
Code 10. Degradable Design	Design for Degradation	Chemical products should degrade safely after use, avoiding persistence.	Designing drugs and polymers that biodegrade after therapeutic effect.	Biodegradable drug-delivery systems based on polylactide-co-glycolide (PLGA) exemplify this code.
Code 11. Real-Time Analysis	Real-Time Monitoring	Analytical techniques should allow real-time monitoring and control to prevent pollution.	Applying in-process controls to adjust conditions and reduce waste.	Use of Process Analytical Technology (PAT) in pharma improves quality and reduces rejects.
Code 12. Inherent Safety	Accident Prevention	Processes should minimize potential for accidents such as leaks, fires, or explosions.	Designing inherently safer chemical processes with low-risk materials.	Continuous flow reactors reduce hazards compared to batch synthesis of active ingredients.

Microwave-assisted technology represents an innovative and promising approach to green synthesis, offering a cost-effective and energy-efficient method that is gaining widespread popularity in pharmaceutical applications [26].

By utilizing microwave irradiation as an alternative energy source, various organic reactions can be completed within minutes, as opposed to requiring hours or even days. Microwave heating involves the transformation of microwave energy into thermal energy through the interaction of molecules with alternating electromagnetic radiation. This radiation spans wavelengths between 0.001 to 1 m and operates at frequencies ranging from 0.3 to 300 GHz. The heating process is primarily driven by two mechanisms: ionic conduction and dipole polarization [27–29].

The synthesis of drug substances using microwave irradiation largely depends on the ability of the reaction medium to efficiently absorb microwave energy and the appropriate selection of solvents to facilitate the synthetic process [30].

In organic synthesis, polar organic solvents such as DMF, DMA, DMSO, N-Methyl-2-pyrrolidone (NMP), methanol, ethanol, and acetic acid are commonly used due to their polarity. Additionally, solvents with high boiling points are preferred, as they allow for a substantial acceleration of the reaction rate [31]. On the other hand, non-polar solvents like toluene, dioxane, and THF can only be utilized in scenarios where other components of the reaction mixture interact with microwave energy, as non-polar molecules are unresponsive to microwave dielectric loss [32].

Microwave-assisted heating in pharmaceutical synthesis

The advantages of employing microwave (Microwave (MW)) heating in chemical synthesis have been highlighted in many studies, including rapid volumetric heating, accelerated reaction rates, improved selectivity, reduced reaction time, lower cost, and higher product yields [32–36].

For instance, GopinadhMeera and colleagues synthesized nitrogen-based five-membered heterocycles—such as pyrroles, pyrrolidines, fused pyrazoles, fused isoxazoles, and indoles—through Microwave (MW)-assisted techniques. Their results showed that compared with conventional methods, microwave-based protocols provided cleaner reactions, shorter processing times, higher compound purity, and greater yields [37].

Similarly, Bimal Krishna Banik's group demonstrated that synthesizing heterocycles like oxadiazole derivatives under microwave irradiation offers notable benefits: very short reaction durations, excellent yields, and simplified purification when compared to traditional synthesis. Furthermore, the volume of solvents required was significantly lower, making the process eco-friendlier [31]. Ivan Ristić and his team also successfully applied microwave methods to produce sodium alginate–chitosan hydrogels, further validating it as a sustainable and environmentally friendly synthesis

approach [38]. Beyond pharmaceutical manufacturing, Microwave (MW) technology also aids in pharmaceutical waste treatment. Tang's group used specialized microwave irradiation to modify MnOx samples, creating oxygen vacancies that enhanced oxygen storage and reducibility. This boosted the breakdown of airborne pollutants. Notably, microwave-synthesized MnCo2O4.5 showed higher catalytic activity than materials made via conventional hydrothermal synthesis due to more abundant oxygen vacancies generated by localized "hotspots" [39].

Manganese-based catalysts with oxygen vacancies are particularly valuable for green pharmaceutical waste management, as they can efficiently degrade pollutants through advanced oxidation methods such as catalytic ozonation and Fenton-like reactions.

Overall, microwave heating is recognized as a straightforward, cost-effective, and powerful technique in applied medicinal chemistry. It not only improves efficiency while lowering waste and reagent use, but also saves energy and promotes sustainable, high-throughput approaches for drug discovery and production. While scale-up challenges remain due to the technical limits of microwave heating in large-scale applications, numerous studies have proposed effective solutions [40, 41]. Thus, Microwave (MW) technology continues to be a vital tool for advancing pharmaceutical synthesis.

Catalysis

Catalysis is a cornerstone of chemical manufacturing, driving the assembly of complex molecules while supporting eco-conscious production methods [42]. Catalytic agents facilitate site-specific transformations and provide diastereoselective control in multifunctional compounds, thereby improving product selectivity. In addition, catalysts enable reactions to proceed under milder, less energy-intensive conditions, making catalytic processes more sustainable. n pharmaceutical manufacturing, transition-metal-catalyzed cross-coupling reactions are widely applied in both drug discovery and large-scale production [43–45]. Despite their utility, many catalytic processes rely on metals that are expensive, potentially toxic, supply-sensitive, or environmentally burdensome to extract—palladium-catalyzed couplings being a classic example [46–50]. These methods have yielded remarkable outcomes; for instance, the Suzuki cross-coupling reaction was successfully employed in the synthesis of abemaciclib, a CDK 4/6 inhibitor used against HR+/HER2-positive metastatic breast cancer [51, 52]. Nonetheless, concerns over the scarcity of platinum-group elements have prompted efforts to develop alternative catalysts based on more abundant, low-cost, and eco-friendly metals. Nickel [53–55], copper [56, 57], and iron [58, 59] catalysts are gaining attention due to their affordability, reduced toxicity, reactivity, and sustainability. For example, Garg *et al.* demonstrated the utility of nickel-based catalysis in the Suzuki–Miyaura coupling of aryl halides and phenolic derivatives using nicotinamide as a ligand in green solvents, achieving high yields of biaryl compounds [60]. Other innovations include photocatalytic and transition-metal-assisted strategies for synthesizing β-lactams, a vital antibiotic class [61]. Oddy and colleagues developed a visible-light-driven approach, enabling intramolecular hydrogen atom transfer to generate β-lactams from acrylamide precursors—an efficient, mild, and atom-economical route [62]. Similarly, the synthesis of N-heterocycles, another critical pharmacophore, has benefited from green catalytic strategies, such as recyclable catalysts, one-pot methodologies, and acceptorless coupling, all of which enhance atom economy while minimizing hazardous waste [63].

Biocatalysis

Biocatalysis, or enzyme-mediated catalysis, has emerged as a sustainable technology in recent decades [64, 65]. It involves using enzymes or whole cells to accelerate chemical reactions [66], offering key advantages: aqueous media, exceptional selectivity, and metal-free products [67]. This approach is already well-established in the industrial production of Active Pharmaceutical Ingredient (API)s [64, 68]. Notable examples include the biocatalytic synthesis of sitagliptin (Januvia), atorvastatin (Lipitor), rosuvastatin (Crestor), and montelukast (Singulair) [69]. Merck's enzyme-catalyzed sitagliptin process improved yield by 10% and productivity by 53%, while eliminating the need for costly, toxic heavy-metal catalysts [70–72]. Similarly, Codexis and Merck scaled up a monoamine oxidase (MAO)-catalyzed desymmetrization to access a bicyclic proline intermediate for boceprevir, a hepatitis C protease inhibitor, cutting both reaction time and waste [73, 74]. Another example is the biosynthetic production of simvastatin, which leverages continuous processing, lowers costs, reduces risk, and minimizes waste [75–77]. More recently, the application of ketoreductases (KREDs) in the synthesis of ipatasertib (an Akt inhibitor) achieved an 56% yield while recycling NADPH, further improving sustainability [78, 79]. Although challenges such as enzyme costs and limited scalability remain [80], the adoption of biocatalysis promotes greener, safer, and more cost-efficient production routes, reinforcing its potential as a mainstream tool in pharmaceutical chemistry.

Green solvents

The pharmaceutical sector relies heavily on solvents, which contribute to over 60% of material use and waste [30]. Shifting toward green solvents—such as glycerol, ethanol, ethyl lactate, water, supercritical CO_2 (Supercritical Carbon Dioxide ($scCO_2$)), and ionic liquids (ILs)—offers significant environmental and economic benefits [32–54].

Water

Despite solubility limitations, water remains a cornerstone green solvent thanks to its non-toxicity, safety, affordability, and availability [55]. In the synthesis of ABT-546, water as a cosolvent enabled a 66% yield without additional extraction steps [77]. Similarly, Takeda Pharmaceuticals developed a nearly water-based process for TAK-644, reducing input materials by 77%, organic solvent use by 64%, and overall water use by 48%, while boosting yield from 35% to 56% [56].

Supercritical carbon dioxide ($scCO_2$)

Supercritical Carbon Dioxide ($scCO_2$) is a promising alternative due to its non-toxic, non-flammable, and readily available nature [56, 56]. It has been shown to modify drug crystallization patterns, producing different polymorphs [59]. $scCO_2$ also serves in supercritical fluid extraction, as demonstrated by Sapkale *et al.*, who isolated tocopherols, phytosterols, and fatty acids from sorghum with pharmaceutical potential [56].

Ionic liquids (ILs)

Ionic Liquid (IL)s are salts liquid at temperatures below 67 °C, consisting of organic cations and inorganic/organic anions [59, 61]. They possess low volatility, thermal stability, conductivity, and excellent solvation abilities, making them valuable for catalysis, separations, and drug formulation.

Challenges include biocompatibility and stability issues [61], yet Ionic Liquid (IL)s hold promise for enhancing drug solubility, bioavailability, and delivery [63]. For instance, N-acetyl amino acid N-alkyl cholinium ILs boosted the solubility of paracetamol and diclofenac by up to fourfold compared to water [44]. Similarly, Sangiorgi *et al.* showed that ILs and deep eutectic solvents (DESs) significantly improved the oral bioavailability of poorly soluble drugs, supporting their integration into sustainable pharmaceutical manufacturing [35].

Flow chemistry

Flow chemistry—also referred to as continuous flow processing—is the technique of performing chemical reactions within a continuous moving stream rather than the traditional batch mode [62].

This approach can be seamlessly integrated with other enabling technologies, such as microwave irradiation, supported catalysts, inductive heating, photochemistry, electrochemistry, microreactors, novel solvent systems, and even 3D printing. Such combinations pave the way for fully automated, highly efficient, and environmentally sustainable processes [78].

Numerous studies highlight the role of flow chemistry in advancing the sustainable synthesis of active pharmaceutical ingredients (Active Pharmaceutical Ingredient (API)s) [80]. A prime example is imatinib, a therapeutic agent for chronic myeloid leukemia and gastrointestinal stromal tumors, which has been produced using flow systems. Here, an in-line solvent-switching method enabled adjustments to reaction solvents during the continuous process, demonstrating the strength of flow-based techniques for synthesizing challenging or poorly soluble compounds [50].

Similarly, a continuous-flow method for converting dihydroartemisinic acid into artemisinin has proven to be both cost-effective and scalable, thereby ensuring a reliable supply of this essential antimalarial agent [63]. Another case is efavirenz, where a semi-continuous protocol yielded rac-efavirenz in 45% yield across four steps [73]. Moreover, a two-step telescoped continuous flow synthesis of diazepam, a WHO essential medicine, achieved 61% purity with a 66% yield within just 15 min by employing two microreactors operated at 0 °C and 60 °C, with an NH_4Br/NH_4OH solution in the second stage [80].

Future prespective

Future developments in green pharmaceutical chemistry are expected to integrate artificial intelligence (AI) for predictive reaction optimization, enzymatic degradation of persistent plastics, and continuous manufacturing to improve scalability. Addressing regulatory hurdles, reducing initial investment costs, and ensuring industrial scalability remain challenges. Nonetheless, these trends will significantly shape the sustainable future of drug development.

CONCLUSION

This review highlights the profound influence of the 12 Principles of Green Chemistry, originally articulated by Paul Anastas and John Warner, on modern strategies in organic synthesis. These principles have become a guiding framework that has shaped contemporary pharmaceutical and chemical research. The most evident impact is the widespread adoption of catalysis and catalytic methodologies, now central to numerous synthetic protocols across academia and industry. Achievements in this field, driven by collaborations among universities, corporations, and research institutions, underscore remarkable progress while also signaling the challenges still ahead. Importantly, the 12 principles should not be viewed as isolated targets but as a cohesive and interconnected framework. True sustainability can only be achieved by applying the principles collectively, exploiting their mutually reinforcing nature. This systemic perspective promotes transformative innovations rather than incremental improvements. A crucial pillar of green chemistry is the design of safer chemicals, aligning with the broader goals of sustainable development. By minimizing toxicity and reducing ecological burdens, chemists are advancing toward a future where chemicals are safer for both people and the planet. Current advances in greener solvents, energy-efficient synthesis, and biocatalytic methods exemplify this progress.

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ABBREVIATION

API-Active Pharmaceutical Ingredient, CDK-Cyclin-Dependent Kinase, DES-Deep Eutectic Solvent, DMF-Dimethylformamide, DMA-Dimethylacetamide, DMSO-Dimethyl Sulfoxide, IL-Ionic Liquid, KRED-Ketoreductase, MAO-Monoamine Oxidase, MW-Microwave, NADPH-Nicotinamide Adenine Dinucleotide Phosphate (Reduced Form), NMP N-Methyl-2-pyrrolidone, NS_3-Non-Structural Protein 3, $scCO_2$-Supercritical Carbon Dioxide, THF-Tetrahydrofuran, WHO-World Health Organization

AUTHORS CONTRIBUTIONS

Conceptualization and methodology, Ahmed Samy; validation, formal analysis, and writing-original draft preparation, Dalia Gaber; review and editing, Eman Al Johani; collection of data, supervision and project administration, Noha Abdo.

CONFLICTS OF INTERESTS

The authors declare no conflicts of interest.

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