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Green Chemistry and Its Applications: Recent Advances, Sustainable Technologies, and Future Perspectives

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Abstract
Green chemistry has revolutionized the field of chemistry by providing alternative approaches to the design of chemicals, materials, and chemical processes. The shift has been from waste minimization to waste prevention at its very source through enhanced process efficiency and resource conservation. The twelve principles of green chemistry offer a comprehensive perspective on how to design improved chemical products and processes, including the use of less hazardous substances, renewable feedstocks, catalysis, and energy-efficient processes. Green chemistry has enjoyed enormous growth and increased significantly in academic and industrial research in the last two decades. The areas of biocatalysis, continuous-flow processing, mechanochemistry, electrochemistry, photochemistry, renewable feedstocks, green solvents, and data-driven reaction design have witnessed unprecedented levels of interest and research activity at both academic and industrial levels. Metrics of sustainability provide a quantitative basis to compare different synthetic routes and evaluate their environmental impact. This includes atom economy, reaction mass efficiency, E-factor, and process mass intensity, among other related quantities. This review highlights the basic principles and metrics of green chemistry, recent advances in the field of sustainable chemistry, and their applications in the areas of pharmaceuticals, materials, energy, agriculture, and environmental protection. The concept of evaluating green chemistry through a single metric or a limited set of metrics has been critically examined. The environmental impact of a chemical process or product should be evaluated based on a life cycle–based multidisciplinary approach rather than a single metric. Green chemistry in the near future is likely to converge with biotechnology, renewable energy, continuous processing, artificial intelligence, circular chemistry, and life-cycle-assessment-driven product design to usher in a new paradigm in sustainable chemistry.
Keywords: *Green chemistry; atom economy; E-factor; process mass intensity; biocatalysis; renewable feedstocks; green solvents.*

1. Introduction

Chemistry has played a vital role in the development of modern society. Pharmaceuticals, fertilizers, fuels, polymers, coatings, detergents, electronic materials, adhesives, and agrochemicals have all contributed to the advancement of human health, agriculture, technology, and modern materials.

The same chemical processes that led to these breakthroughs can have harmful consequences for the environment. Many chemical manufacturing processes are highly wasteful in terms of reagents, organic solvents, nonrenewable feedstocks, and energy. In addition, multistep syntheses are highly disfavored due to the generation of a significant amount of waste from repetitive extractions, purifications, protection, and deprotection steps. Traditionally, the problems of chemical waste generation and sustainability have been addressed by end-of-pipe treatments in which chemical waste is detoxified and disposed of in the environment. Alternatively, green chemistry proposes that waste prevention at the design stage is far more desirable than waste remediation at the end of the chemical process.

This different philosophical approach has had a profound effect on the way chemical reactions, molecules, and chemical processes have been designed to improve sustainability. As a result, chemical processes today consider the importance of sustainability and waste minimization at the very onset of process design rather than at the end of the reaction when the undesired byproducts and wastes have already formed.

The principles of green chemistry were enunciated by Anastas and Warner in 1998 [1]. The principles span a wide range of ideas related to waste prevention, improvement of atom economy, use of less hazardous substances, design of safer chemicals, safer solvents and auxiliaries, energy efficiency, renewable feedstocks, reduction of derivatization, catalysis, design for degradation, real-time analysis, and inherently safer chemistry.

The atom economy, introduced by Trost [2], is a related concept, in which the percentage yield of the desired product is related to the amount of reactant. Unlike the traditional percentage yield, the atom economy takes into account the atoms of the reactants that are incorporated into the desired product. [Figure 1]

$$AE = \frac{M_r(\text{desired product})}{\sum \nu_i M_r(\text{reactant}_i)} \times 100$$

where M_r is the relative molecular mass and nu_i represents the stoichiometric coefficient.

While an 80% atom economy may seem impressive, such a reaction may generate more waste than a 50% atom economy reaction that does not require large reagent excesses, use of organic solvents, protecting-group chemistry, and drastic reaction conditions. Yield, though important, is only a part of the story. A more complete sustainability assessment considers solvent use, reagent and catalyst requirements, energy consumption, toxicity, and process safety [3-6].

This review covers the fundamental principles of green chemistry, the common metrics used in evaluating chemical processes, and recent advances in green chemistry, along with an outlook on emerging opportunities.

2. Twelve Principles of Green Chemistry

The twelve principles of green chemistry are best used as a conceptual framework rather than a set of hard-and-fast rules. They can guide the decision-making process in designing a molecule or a chemical process, starting from molecular and process design, going through manufacturing and use, and ending with recovery, recycling, and final disposal.

Table **1** provides a summary of the twelve principles of green chemistry and their practical implications.

Table 1. Twelve principles of green chemistry and their practical meaning.

Sr.No.	Principle	Practical meaning
1)	Prevention	Avoid creating waste instead of treating it afterward
2)	Atom economy	Incorporate as much of the starting material as possible into the final product
3)	Less hazardous synthesis	Use and generate substances with lower toxicity
4)	Designing safer chemicals	Maintain useful performance while reducing harmful effects
5)	Safer solvents and auxiliaries	Minimize auxiliary materials and choose safer solvents when needed
6)	Energy efficiency	Reduce unnecessary heating, cooling, pressure, and energy use
7)	Renewable feedstocks	Prefer renewable raw materials where technically and economically practical
8)	Reduce derivatives	Avoid unnecessary protection, deprotection, activation, and temporary modifications
9)	Catalysis	Prefer catalytic methods to stoichiometric reagents
10)	Design for degradation	Design products that break down into safer substances after use
11)	Real-time analysis	Monitor processes during operation to prevent hazardous conditions or products
12)	Inherently safer chemistry	Reduce the risk of fire, explosion, and accidental chemical release

Applying these principles effectively requires judgment, since improving one parameter may not necessarily lead to a better overall process. A solvent that utilizes renewable feedstocks may appear to be a better choice than petroleum-derived alternatives, but the overall environmental impact must also be taken into account, including the materials and energy consumed in its production. Similarly, while solvent-free chemistry avoids using a reaction solvent, the overall process may still involve highly toxic reagents and require extensive purification after the reaction is complete. Thus, a complete evaluation rather than a single metric must be used to analyze the sustainability of a chemical process. The raw materials, reagents, reaction conditions, isolation and purification processes, energy requirements, hazards, and overall waste generation

and the final disposition of the product must all be taken into account when evaluating the sustainability of a chemical process.

3. Quantitative Metrics in Green Chemistry

The ability to assess the sustainability of chemical processes can be enhanced by quantitative evaluation of the different metrics of chemical sustainability. In the absence of quantitative comparisons, it becomes extremely challenging to devise a more sustainable chemical process and identify the changes that may have the most significant impact on sustainability.

A set of sustainability metrics has been developed to provide quantitative measures of different aspects of chemical processes. These include atom economy (AE), reaction mass efficiency (RME), E-factor, and process mass intensity (PMI), which all describe different aspects and provide distinct but complementary information about a particular chemical process.

3.1. Atom Economy

Atom economy describes the efficiency with which the atoms in the reactants are incorporated into the desired product [7-8]. [Figure 1]

$$AE = \frac{M_r(\text{desired product})}{\sum \nu_i M_r(\text{reactant}_i)} \times 100$$

Where M_r represents relative molecular mass.

An ideal reaction would have a 100% atom economy, in which all the atoms from the reactants are incorporated into the product with no stoichiometric waste. Addition and rearrangement reactions tend to have high atom economies, while those that involve large leaving groups typically exhibit lower atom economies.

The advantage of this metric is that it is easy to calculate and can be used to compare different synthetic routes at the very onset of process design. One of the key limitations of AE is that it does not take into account the experimental yield, reagent excess, catalysts, solvents, or other processing materials. Thus, a reaction with a high atom economy can have poor sustainability performance when tested under actual experimental conditions.

3.2. Reaction Mass Efficiency

A related metric, reaction mass efficiency, is calculated using the actual mass of product isolated and the masses of the reactants: [Figure 2]

$$RME = \frac{\text{mass of isolated product}}{\sum \text{mass of reactants}} \times 100$$

Because RME is calculated using the actual experimental performance, it describes an important component of the overall process. However, like AE, it does not account for solvent or other processing materials. Therefore, it reflects only the utilization of the reaction components rather than the overall efficiency of the process.

3.3. E-Factor

The E-factor provides a measure of the amount of waste generated during a chemical process: [Figure 3]

$$E = \frac{\text{total mass of waste}}{\text{mass of product}}$$

A lower E-factor indicates a more efficient chemical process.

The E-factor is particularly useful when comparing different chemical processes that produce the same or similar products. It is also easy to report and communicate. However, like AE, it does not account for the difference between benign and hazardous wastes-wastes that are equally hazardous in their respective forms, but which may have vastly different environmental impacts when released into the environment.

3.4. Process Mass Intensity

Atom economy and related metrics focus on the efficiency with which atoms from reactants are incorporated into the product. The amount of solvent, water, and other materials used in a chemical process are not considered. Process mass intensity (PMI) was developed as a metric to encompass the materials used and provide a more complete sustainability assessment. [Figure 4]

$$PMI = \frac{\text{total mass of materials used}}{\text{mass of product obtained}}$$

The theoretical minimum PMI is 1, which corresponds to a process in which all the components are incorporated into the product with no waste. Actual processes always have values greater than 1 because of the additional reagents, solvents, and processing materials.
From the definitions, we can conclude that

$$PMI = E + 1$$

When applied to pharmaceutical manufacturing, PMI has provided critical insights because it enables us to assess the contribution of individual components such as solvents, reagents, and water to the overall material utilization. Using this metric, it has been found that solvent use, extraction, and washing can be more important than the reaction itself in terms of the overall material balance [9].
Table **2** summarizes the advantages and limitations of AE, RME, E, and PMI. Each of these metrics provides a different piece of information about a chemical process, and all of them should be used in combination to obtain a complete sustainability assessment.

Table 2. Comparison of common green chemistry metrics.

Metric	**Ideal value**	**Main advantage**	**Main limitation Atom economy**
Atom economy	100%	Useful when selecting a synthetic route	Does not account for yield or solvent use
RME	100%	Reflects actual reaction performance	Often excludes solvents
E-factor	0	Gives a simple measure of waste	Does not indicate waste toxicity
PMI	1	Measures overall material consumption	Does not distinguish hazardous from benign inputs

4. Recent Advances in Sustainable Technologies

4.1. Catalysis and Biocatalysis

Catalysis plays a central role in more sustainable chemical production, enabling the use of lower temperatures and pressures, reduced waste, and higher selectivity. Bio- or enzymatic catalysis provides mild reaction conditions and exceptional chemo-, regio-, and stereoselectivity. Directed evolution and protein engineering have enabled the discovery of novel enzymes that catalyze remarkable reactions, ranging from C–H functionalization to complex biosynthetic transformations. This has had a major impact on pharmaceutical synthesis, in which stereoselectivity is critical to the biological activity of a drug. Biocatalysis has been instrumental in the development of a number of blockbuster drugs, including sitagliptin, in which a recombinant transaminase replaced a traditional asymmetric catalytic process [10]. The field has seen rapid advances in computational enzyme design, high-throughput screening and robotics, and experimental optimization to enable the use of biocatalytic transformations beyond their traditional applications in pharmaceutical and fine-chemical synthesis.

4.2. Safer Solvents

A large proportion of the total mass of a chemical process consists of solvents, which can be used during the reaction as well as in the subsequent steps of isolation and purification. Water, ethanol, ethyl acetate, 2-methyltetrahydrofuran, and a number of bio-based solvents are some of the possible alternatives, depending on the nature of the process.
Thus, a truly sustainable process cannot be based on a single solvent system. The safety and sustainability of a solvent must be evaluated on a case-by-case basis, taking into account its toxicity, flammability, chemical stability, availability, environmental persistence, production process, and recyclability, as well as the energy required for its recovery and treatment [11]. The most sustainable option will depend on the specific chemical process.

4.3. Mechanochemistry

Mechanochemistry provides an alternative to conventional solution-based chemical synthesis by using mechanical energy in the form of ball milling or extrusion to promote chemical reactions. One of the most important advantages of mechanochemistry is that it can reduce or eliminate the use of bulk solvents in chemical synthesis, resulting in reduced waste and energy consumption associated with solvent recovery and treatment. A solvent-free reaction is not necessarily

sustainable, however, since the mechanical ball-milling process itself can be energy intensive, and the reaction product may require further processing and purification before it can be isolated.

Despite these challenges, mechanochemistry has been combined with continuous processing to achieve solvent-free production of triacetin from glycerol using a complementary mechanochemical biphasic and catalytic approach through ICHeM technology [12]. This is just one example of a rapidly growing number of mechanochemical processes that have moved from the research lab to pilot-scale manufacturing.

4.4. Continuous-Flow Chemistry

Continuous-flow chemistry replaces the traditional batch process with continuous feeding and removal of reactants and products. The process can be carried out in tubular or continuously stirred tank reactors, extruders, or any other type of reactor configuration. Flow reactors offer excellent control over temperature, pressure, mixing, and residence time, and they are especially well suited for highly exothermic reactions and transformations that involve unstable, hazardous, or highly reactive intermediates. Integration with real-time analytics and advanced process control has further improved the performance of flow chemistry, enabling rapid and informed decision-making based on in situ analysis of the reaction.

Nevertheless, the environmental benefit of a continuous-flow process must be evaluated in the context of the overall manufacturing process, rather than a single unit operation. An improved reactor does not necessarily reduce the overall environmental footprint if the downstream process produces significant amounts of waste.

4.5. Electrochemistry and Photochemistry

Electrochemistry provides an alternative to conventional stoichiometric oxidation and reduction reactions by using electricity to drive the electron transfer process. The ability to replace stoichiometric oxidants and reductants with electricity opens the door to a major reduction in reagent and waste consumption. The environmental benefit is further enhanced if the electricity is produced from renewable resources through photovoltaics or other means.

Photochemistry is another promising area that enables the use of light in chemical transformations through modern photocatalytic reactions. The combination of light and electricity has led to the emergence of new photoelectrochemical technologies, which are being investigated for a wide range of applications, from hydrogen production and solar fuels to carbon dioxide utilization in the production of valuable chemicals. Overall, these technologies hold great promise but must be evaluated within the context of practical implementation, including the sustainability of the overall process and the energy requirements.

4.6. Renewable Feedstocks

The replacement of fossil feedstocks with renewable feedstocks is an important goal in sustainable chemical production. A number of cellulose-based feedstocks, including lignin, starch, vegetable oils, terpenes, glycerol, biomass, waste-derived carbon, and fermentation products, can be used to produce liquid fuels, polymers, solvents, and other products through chemical transformations. Life-cycle analysis must be performed to ensure that the overall process does not consume excessive amounts of water, fertilizers, land, or energy during cultivation or transportation. Its impact on food supply and sustainability must also be carefully evaluated before it can be considered a truly sustainable option.

5. Applications of Green Chemistry

Green chemistry has had a major impact on research and development across a wide range of industries.

5.1. Pharmaceuticals

Pharmaceutical production often involves complex multistep syntheses that involve a large number of reagents, solvents, processing materials, and energy. PMI analysis has helped identify the different stages of a pharmaceutical process, and opportunities for improvement can be identified once the weak links in the process have been identified. Such opportunities include switching to greener solvents or reaction conditions, telescopization of certain steps, the use of catalysis or biocatalysis, improved crystallization methods, and the use of continuous-flow processing for suitable reactions.

Because the solvent and isolation and purification processes often contribute to a disproportionately large share of the overall PMI in a pharmaceutical process, changes to these steps may offer the biggest improvements in sustainability.

5.2. Polymers and Materials

Green chemistry has also had a major impact on polymer and materials chemistry. The life cycle of a polymer, beginning with its production and continuing through its use and eventual disposal, is receiving increased attention, and processes such as repair, reuse, recycling, and biodegradation are being considered.

5.3. Energy and Environmental Protection

Chemistry has contributed to a number of energy technologies by providing innovative materials for hydrogen production, low-carbon and carbon-negative fuels, advanced battery materials, water-treatment chemicals, and materials for carbon capture and air and water purification. The replacement of rare elements with more abundant ones in heterogeneous catalysts will also help to reduce the environmental impact of certain processes. Electrochemical and photoelectrochemical technologies provide an additional opportunity to harness renewable electricity or light for chemical production.

5.4. Agriculture

Agricultural chemistry is another area in which green chemistry has made a significant impact. A number of sustainable agricultural practices are being developed. These include the production of renewable feedstocks, such as cellulosic ethanol, and the development of less hazardous pesticides and fertilizers. Green chemistry has further helped reduce the environmental impact of the fertilizers, herbicides, insecticides, and fungicides used in agriculture.

6. Conclusion

Green chemistry has transformed chemical production by introducing a new philosophy in which chemical processes are designed with sustainability in mind. A number of principles and practical approaches have been developed to guide the design of greener chemical processes. The use of novel metrics such as atom economy, reaction mass efficiency, E-factor, and PMI has enhanced our ability to evaluate chemical processes and identify opportunities for improvement. Recent advances in catalysis, biocatalysis, continuous-flow processing, mechanochemistry, electrochemistry, and photochemistry have further improved the sustainability of chemical production. The application of these concepts has had a major impact not only in the pharmaceutical industry but also in other areas of chemical production such as polymers, energy, and materials. The outlook for green chemistry is highly promising, as it is set to converge with related technologies to create new paradigms in sustainable chemical production.

References

[1] Anastas, P.T.; Warner, J.C. Green Chemistry: Theory and Practice. Oxford University Press, New York, 1998.
[2] Trost, B.M. The atom economy—A search for synthetic efficiency. Science 1991, 254, 1471–1477.
[3] Sheldon, R.A. Fundamentals of green chemistry: Efficiency in reaction design. Chem. Soc. Rev. 2012, 41, 1437–1451.
[4] Constable, D.J.C.; Curzons, A.D.; Cunningham, V.L. Metrics to ‘green’ chemistry—Which are the best? Green Chem. 2002, 4, 521–527.
[5] Jiménez-González, C.; Ponder, C.S.; Broxterman, Q.B.; Manley, J.B. Using the right green yardstick: Why process mass intensity is used in the pharmaceutical industry to drive more sustainable processes. Org. Process Res. Dev. 2011, 15, 912–917.
[6] Jiménez-González, C.; Constable, D.J.C.; Ponder, C.S. Evaluating the “greenness” of chemical processes and products in the pharmaceutical industry: A green metrics primer. Chem. Soc. Rev. 2012, 41, 1485–1498.
[7] Prat, D.; Wells, A.; Hayler, J.; Sneddon, H.; McElroy, C.R.; Abou-Shehada, S.; Dunn, P.J. CHEM21 selection guide of classical- and less classical-solvents. Green Chem. 2016, 18, 288–296.
[8] Fantozzi, N.; Volle, J.-N.; Porcheddu, A.; Virieux, D.; García, F.; Colacino, E. Green metrics in mechanochemistry. Chem. Soc. Rev. 2023, 52, 6680–6714.

[9] McElroy, C.R.; Constantinou, A.; Jones, L.C.; Summerton, L.; Clark, J.H. Towards a holistic approach to metrics for the 21st century pharmaceutical industry. Green Chem. 2015, 17, 3111–3121.
[10] Buller, R.; Lutz, S.; Kazlauskas, R.J.; Snajdrova, R.; Moore, J.C.; Bornscheuer, U.T. From nature to industry: Harnessing enzymes for biocatalysis. Science 2023, 382, eadh8615.
[11] Savile, C.K.; Janey, J.M.; Mundorff, E.C.; et al. Biocatalytic asymmetric synthesis of sitagliptin manufacture. Science 2010, 329, 305–309.
[12] Nguyen, R.; Halloumi, S.; Malpartida, I.; Len, C. Solvent-free production of triacetin from glycerol through complementary mechanochemical, biphasic, and catalytic approaches using ICHeM technology. Org. Process Res. Dev. 2025, 29, 769–777.