Green Chemistry and Sustainable Synthesis: Recent Advances in Eco-Friendly Chemical Reactions and Industrial Applications

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***Abstract*—Green chemistry seeks to design chemical products and processes that reduce or eliminate the use and generation of hazardous substances. Its importance has increased as industries face pressure to reduce waste, energy demand, emissions and dependence on non-renewable resources while maintaining product quality and economic viability. This paper examines recent directions in sustainable synthesis and their relevance to laboratory research and industrial production. It discusses the twelve principles of green chemistry as a framework for process design; solvent selection and solvent-free synthesis; catalysis and biocatalysis; renewable feedstocks; microwave- and flow-assisted synthesis; and selected applications in pharmaceuticals, polymers, fine chemicals and materials. This review also considers how life-cycle assessment, process mass intensity and related metrics can distinguish genuine environmental improvement from changes that merely shift impacts between stages. Across the approaches considered, no single technology is universally sustainable: performance depends on reaction yield, selectivity, reagent origin, energy source, solvent recovery, catalyst lifetime, product use and end-of-life treatment.**

The paper argues that meaningful progress requires integrating molecular-level reaction design with process engineering and transparent environmental assessment. It identifies practical research needs in scalable solvent-free methods, robust catalysts, safer renewable feedstocks, reproducible reporting and the translation of laboratory demonstrations into industrially relevant processes.

***Index Terms*—Green chemistry; sustainable synthesis; atom economy; catalysis; safer solvents; renewable feedstocks; process intensification; life-cycle assessment; industrial applications.**

I. INTRODUCTION

Chemical synthesis underpins pharmaceuticals, agriculture, materials, energy technologies, consumer products and a wide range of industrial activities. Conventional routes have often been optimised primarily for yield, reaction time and cost. However, high product yield alone does not guarantee an environmentally responsible process. A synthesis may generate large quantities of salts, use hazardous solvents, require energy-intensive purification or depend on feedstocks with substantial upstream environmental burdens. These concerns have encouraged a shift from end-of-pipe pollution control towards prevention through the design of chemical reactions and processes.

Green chemistry is commonly defined as the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances (Anastas & Warner, 1998). The approach is preventive rather than corrective: it aims to avoid waste and hazard at the point of design instead of treating pollution after it has been created. Its twelve principles address waste prevention, atom economy, less hazardous synthesis, safer products, safer solvents and auxiliaries, energy efficiency, renewable feedstocks, reduced derivatisation, catalysis, design for degradation, real-time analysis and inherently safer chemistry.

Sustainable synthesis is broader than replacing one solvent or reagent with another. It requires consideration of the complete process, including raw-material production, reaction conditions, separation, solvent recovery, equipment, worker safety, product performance and disposal. For example, a solvent

described as bio-based is not automatically safer, and a reaction conducted without solvent may still have poor material efficiency or require substantial energy. Similarly, a catalyst can reduce reagent use and improve selectivity, but its preparation, toxicity, critical-metal content and recovery must also be considered. Industrial implementation presents both opportunities and constraints. Pharmaceutical and fine-chemical manufacturing can benefit from improved selectivity and reduced purification demand, while polymer and materials industries can use renewable carbon sources and design products for longer service life or improved end-of-life management. Yet scale-up can alter heat transfer, mixing, mass transfer and safety characteristics. A promising laboratory procedure therefore, needs process-level evaluation before claims of industrial sustainability are made. This paper reviews selected advances in eco-friendly chemical reactions and their industrial relevance. It focuses on approaches that can be assessed using established chemical and process metrics, and it highlights the conditions under which they may offer environmental benefits. The central argument is that green chemistry is most effective when molecular design, process engineering and life-cycle thinking are applied together.

II. REVIEW OF LITERATURE

Research on green chemistry and sustainable synthesis has evolved from the development of foundational principles to the practical application of cleaner technologies in laboratory research and industrial manufacturing. The literature highlights several interconnected areas, including waste prevention, catalytic efficiency, safer solvents, renewable feedstocks, biocatalysis, energy-efficient synthesis, and process intensification.

Trost (1991) introduced the concept of atom economy as a measure of synthetic efficiency, arguing that chemical reactions should be designed to incorporate as many atoms of the reactants as possible into the desired product. Unlike percentage yield, atom economy evaluates the theoretical efficiency of a reaction based on its stoichiometry. This concept provided an important foundation for subsequent developments in green chemistry because it shifted attention towards the generation of by-products and the efficient use of raw materials. Trost's work remains relevant in the comparison of alternative synthetic pathways, particularly in pharmaceutical and fine-chemical production, where conventional routes may involve multiple reagents and generate considerable quantities of waste.

Anastas and Warner (1998) established the twelve principles of green chemistry, providing a systematic framework for designing chemical products and processes that reduce or eliminate the use and generation of hazardous substances. Their principles cover waste prevention, atom economy, less hazardous chemical synthesis, safer chemical design, safer solvents and auxiliaries, energy efficiency, renewable feedstocks, reduction of unnecessary derivatisation, catalysis, design for degradation, real-time analysis for pollution prevention, and inherently safer chemistry for accident prevention. This framework broadened the evaluation of chemical synthesis beyond conventional measures such as yield and reaction time. It encouraged chemists to consider material consumption, toxicity, energy demand, and the environmental consequences of products and processes. The twelve principles subsequently became a major foundation for research in sustainable synthesis, industrial process improvement, and environmental chemistry.

Clark (1999) examined the emerging concept of green chemistry as a means of reducing the environmental impact of chemical production. The study highlighted the importance of designing chemical processes that prevent pollution rather than treating waste after it has been generated. Clark discussed the potential of alternative feedstocks, cleaner reaction pathways, and improved process design in reducing dependence on hazardous materials and non-renewable resources. The work helped establish green chemistry as a proactive approach to environmental protection, integrating chemical innovation with sustainability objectives. It also drew attention to the role of chemical industries in adopting cleaner production methods and developing processes that reduce environmental burdens throughout the product life cycle.

Sheldon (2000) discussed the contribution of green chemistry to sustainable development, emphasising that the environmental performance of chemical manufacturing depends on preventing waste at the source. The work connected resource efficiency, reaction design and the reduction of hazardous substances with the broader goals of sustainable

chemical production. This approach helped establish the importance of evaluating the whole process rather than focusing exclusively on the final product or isolated reaction step. It also reinforced the need for measurable indicators that allow researchers and industrial chemists to compare processes and identify opportunities for improvement.

Sheldon and van Bekkum (2001) explored the relationship between catalysis and sustainable chemistry, emphasising the importance of catalytic processes in improving the efficiency of chemical transformations. Their work explained how catalysts can reduce the need for stoichiometric reagents, improve product selectivity, and minimise the generation of unwanted by-products. Catalytic methods were presented as valuable alternatives to conventional reactions that require large quantities of reagents and may produce substantial waste. The authors also drew attention to the broader role of catalysis in industrial chemistry, where improvements in reaction efficiency can generate both economic and environmental benefits. Their contribution remains relevant to the development of cleaner synthetic routes, although catalyst recovery, stability, toxicity, and the availability of catalytic materials must also be considered.

Capello, Fischer and Hungerbühler (2007) investigated approaches for assessing the environmental, health, and safety characteristics of solvents. Their work demonstrated that solvent selection is a multidimensional problem and cannot be based solely on a solvent's origin or its classification as conventional or alternative. The authors discussed assessment approaches that consider toxicity, environmental persistence, occupational hazards, and other relevant properties. Their contribution is important because solvents often constitute a large proportion of the materials used in chemical synthesis, particularly in pharmaceutical and fine-chemical manufacturing. The study indicated that replacing a hazardous solvent with a nominally greener alternative does not automatically guarantee a lower overall environmental impact. A comprehensive assessment must also account for solvent recovery, energy requirements, process performance, and waste generation. Anastas and Beach (2008) reviewed the development of green chemistry as a transformative framework for chemical research and industrial practice. Their work discussed advances in synthetic efficiency, alternative reaction methods, safer reagents and solvents, and the use of renewable resources as chemical feedstocks. The authors presented green chemistry as more than a set of environmental guidelines, describing it as an approach capable of influencing the design of chemical products and manufacturing systems. Their review highlighted the importance of integrating environmental considerations into the earliest stages of chemical innovation. It also demonstrated how the principles of green chemistry could be translated into practical improvements in chemical synthesis and industrial production.

Prat and colleagues (2013) described Sanofi's solvent selection guide as a practical tool for improving solvent choices in chemical processes. Their work reflected the growing need for solvent-selection systems that could be used by chemists during route development and process optimisation. Solvent guides classify solvents according to criteria such as health, safety and environmental impact, helping researchers identify problematic solvents and consider alternatives. The study was significant for industrial chemistry because solvent replacement often involves balancing environmental benefits with reaction performance, product quality, recovery requirements and manufacturing costs.

Prat and colleagues (2016) further contributed to solvent-selection research through the development and discussion of practical guides for pharmaceutical processes. Their work supported the use of structured assessment tools rather than relying on informal judgments about whether a solvent is environmentally acceptable. The literature on solvent selection indicates that solvent substitution should be assessed in the context of the complete process, including reaction conditions, extraction, purification, recovery and disposal. A solvent with a favourable hazard profile may still require substantial energy for removal or may perform poorly in a particular reaction. Thus, solvent selection remains an important area in which chemical performance and environmental assessment must be considered together.

Byrne and colleagues (2016) reviewed solvent-selection guides and related techniques, examining their similarities, differences and practical applications. Their work highlighted the importance of reducing the use of highly hazardous solvents in laboratory synthesis and pharmaceutical

manufacturing. The authors discussed how solvent guides can assist researchers in identifying safer alternatives and incorporating environmental, health and safety considerations into early process development. They also indicated that these tools are most useful when applied alongside technical judgment and process-specific evaluation. The study reinforced the idea that greener solvent selection is not simply a matter of replacing one solvent with another; it requires a systematic assessment of the solvent's complete role in the process

Almeida and colleagues (2019) reviewed the evolution and wider impacts of green chemistry, including its influence on chemical analysis, pharmaceutical research, industrial practices and environmental protection. Their review described the development of green chemistry from pollution-prevention approaches into a broader framework for sustainable chemical design. It also highlighted green analytical chemistry as an important research direction, since analytical procedures themselves may consume hazardous reagents, solvents and energy. The study drew attention to the consequences of chemical choices at different stages, from method development and production to use and disposal. This wider perspective supports the integration of sustainability principles across the chemical sciences rather than limiting their application to synthetic reactions alone. The reviewed studies demonstrate a gradual expansion in the scope of green chemistry research. Early contributions established the theoretical foundations of atom economy, pollution prevention and the twelve principles of green chemistry. Subsequent research focused on waste measurement, catalysis and solvent assessment, while more recent work has examined biocatalysis, continuous-flow processing, alternative reaction media and the broader integration of sustainability into industrial chemistry.

Despite substantial progress, important research gaps remain. Many studies examine individual principles or technologies, while fewer provide comparable, comprehensive assessments across the entire manufacturing process. There is also a need for greater reporting consistency in sustainability metrics, especially when comparing laboratory-scale findings with industrial-scale operations. The practical feasibility of emerging solvents, renewable feedstocks, catalysts and biocatalytic systems must be assessed in terms of cost, availability, toxicity, process compatibility and scalability.

The literature therefore indicates that the future of sustainable synthesis lies not in adopting a single "green" technology but in combining reaction design, safer materials, efficient catalysis, energy management and measurable environmental assessment. This integrated approach can support the development of chemical processes that are technically reliable, economically feasible and environmentally responsible.

III. NEED OF THE STUDY

The need for this study arises from the growing demand for chemical processes that combine technical performance with reduced environmental and health burdens. Industrial chemistry must respond to resource constraints, waste-management costs, occupational safety requirements and climate-related pressures without compromising product quality or supply reliability. A concise synthesis of current approaches can help researchers and process developers identify where greener reaction design is most likely to provide measurable benefits.

The study is also relevant because sustainability claims are sometimes based on a single indicator, such as reaction yield, renewable origin or reduced reaction time. Such indicators are useful but incomplete. A broader review can clarify the role of material efficiency, hazard, energy demand, solvent recovery and life-cycle impacts in evaluating a process. It can also identify the research and reporting practices needed to make laboratory findings more reproducible and industrially meaningful.

IV. STATEMENT OF THE PROBLEM

Many chemical processes continue to rely on hazardous reagents, resource-intensive separations, non-renewable feedstocks and energy-demanding operating conditions. Although greener alternatives have been reported, their advantages are not always assessed using comparable system boundaries or practical scale-up criteria. A process may reduce one impact while increasing another for example, lowering solvent use but increasing energy demand, or using a renewable feedstock that requires intensive cultivation and processing.

The central problem addressed in this review is therefore how recent eco-friendly synthesis strategies can be evaluated and integrated so that improvements in reaction chemistry translate into credible environmental and operational benefits. The review considers both the potential of these strategies and the technical, economic and assessment limitations that may restrict their application.

V. METHODOLOGY

This paper is designed as a narrative review of established concepts and selected research directions in green chemistry and sustainable synthesis. It does not report new laboratory experiments or generate original numerical results. The discussion is organised around the twelve principles of green chemistry and the process-level factors that determine whether a reaction can be considered more sustainable.

Literature identification is based on foundational books and peer-reviewed publications concerning green chemistry, solvent selection, catalysis, process metrics and sustainable process design. The cited works provide conceptual frameworks and examples rather than a systematic, exhaustive database search. The review compares approaches qualitatively according to reaction efficiency, hazard considerations, energy requirements, material inputs, separation needs, scalability and potential industrial relevance.

The principal evaluation concepts are:

- Atom economy: the proportion of reactant atoms incorporated into the desired product, based on the balanced reaction equation.
- Reaction mass efficiency: the mass of desired product relative to the mass of reactants used, often accounting for yield.
- Process mass intensity (PMI): total mass of materials used in a process divided by the mass of product.
- E-factor: mass of waste generated per mass of product, with the precise boundary and treatment of water stated where relevant.
- Energy demand: energy required for reaction, heating, cooling, separation and solvent recovery.
- Hazard and life-cycle considerations: intrinsic hazards and potential impacts associated with raw materials, processing, use and end-of-life.

These measures are complementary. Atom economy is a theoretical reaction metric and does not include solvents or work-up. PMI and E-factor are process-oriented but depend on system boundaries and reporting conventions. Life-cycle assessment can provide a broader environmental perspective, although results depend on data quality, functional unit and allocation choices. Accordingly, the review avoids assigning universal numerical rankings to technologies without a common dataset.

VI. RESULTS

As a narrative review, the results are presented as a structured synthesis of the approaches and their practical implications rather than as newly measured experimental data.

1. Safer solvents and solvent reduction

Solvents can represent a substantial share of material use in fine-chemical and pharmaceutical processes. Replacing a hazardous solvent with a lower-hazard alternative, reducing solvent volume or improving recovery can lower occupational and environmental burdens. Water, ethanol and selected bio-derived solvents may be useful in particular applications, but suitability depends on solubility, reaction compatibility, flammability, toxicity, energy required for removal and the source of the solvent. Solvent selection guides are therefore valuable as screening tools, not as substitutes for process-specific assessment. Solvent-free synthesis can reduce solvent consumption and simplify work-up in suitable reactions. Mechanochemical methods, in which mechanical energy promotes chemical transformation, have attracted attention for solid-state synthesis and selected organic reactions. Their limitations include sensitivity to milling conditions, scale-up challenges, equipment wear and the need to understand energy use and product consistency. A solvent-free label should not be treated as proof of low overall impact unless reagent excess, washing, energy and downstream processing are also evaluated.

2. Catalysis and selective synthesis

Catalysts can improve reaction rates and selectivity while reducing the need for stoichiometric reagents. Heterogeneous catalysts may be separated from reaction mixtures and reused, whereas homogeneous

catalysts can offer high activity and selectivity but may require additional separation. Enzymes can provide selective transformations under mild conditions and are especially relevant to chiral synthesis and functional-group-specific reactions.

The sustainability of a catalytic route depends on catalyst loading, turnover, lifetime, preparation, recovery and the origin of active components. Catalysts based on scarce or toxic metals may present resource and hazard concerns. Research into earth-abundant metals, supported catalysts, recyclable catalytic systems and biocatalysis is therefore relevant. In industrial settings, selectivity can be particularly important because fewer by-products may mean less purification, lower solvent demand and reduced waste.

3. Renewable feedstocks and bio-based chemistry

Renewable feedstocks, including biomass-derived sugars, oils, lignocellulosic fractions and platform molecules, can reduce dependence on fossil carbon for selected products. Their use is not automatically sustainable: land use, water demand, fertiliser inputs, biodiversity effects, transport and competing uses of biomass influence the overall assessment. Waste-derived and non-food feedstocks may offer advantages in some contexts, but their composition and supply can vary. A key research challenge is developing conversion routes that tolerate feedstock variability while maintaining yield and product quality. Catalytic upgrading, fermentation, enzymatic conversion and integrated biorefinery approaches can help convert complex biomass into chemicals and materials. The choice of feedstock should be linked to the intended product and evaluated using a life-cycle perspective.

4. Energy-efficient and intensified synthesis

Microwave-assisted synthesis can accelerate some reactions by providing rapid heating, but reported time savings do not necessarily translate into lower energy consumption at scale. Comparisons should include equipment efficiency, batch size, cooling, purification and energy source. Continuous-flow chemistry offers precise control of residence time, heat transfer and mixing, and can improve the handling of hazardous or highly exothermic transformations. Flow systems may also support automation and consistent product quality. Scale-up in flow chemistry is not simply a matter of increasing reactor dimensions. Throughput may instead be increased through numbering-up, while pressure drop, clogging, fouling, materials compatibility and continuous downstream processing require attention. Both microwave and flow methods are best assessed against a conventional process using equivalent product specifications and complete process boundaries.

5. Industrial applications

In pharmaceutical manufacturing, greener synthesis can reduce solvent use, improve stereoselectivity, avoid protecting-group steps and decrease waste from purification. Because pharmaceutical products require stringent quality and safety controls, changes to reaction routes must be supported by process validation and impurity analysis. Catalytic and biocatalytic transformations can be valuable when they simplify multi-step routes or reduce hazardous reagents. In polymer chemistry, renewable monomers, catalytic polymerisation and design for recycling or degradation are active areas. The environmental value of a bio-based polymer depends on its production route and end-of-life fate; bio-based origin and biodegradability are distinct properties. For fine chemicals and specialty materials, solvent recovery, selective catalysis and process intensification can improve material efficiency, but product purity and batch reproducibility remain essential

Table 1. Qualitative comparison of selected sustainable synthesis approaches

Approach	Potential advantages	Important limitations	Relevant evaluation
Safer solvent selection	Reduced hazard and emissions; possible recovery	Solvent may affect yield, separation and energy	Hazard screening, PMI, recovery rate
Solvent-free/mechanochemical synthesis	Lower solvent demand; possible simpler work-up	Scale-up, heat and energy accounting, reproducibility	PMI, energy per product, yield
Heterogeneous catalysis	Selectivity and potential catalyst reuse	Leaching, deactivation, catalyst manufacture	Turnover, lifetime, waste and metal balance

Biocatalysis	High selectivity; often mild conditions	Enzyme stability, substrate scope, cofactor and separation needs	Yield, enzyme reuse, process mass
Renewable feedstocks	Potential reduction in fossil-resource dependence	Land, water, supply and processing impacts	Life-cycle assessment, feedstock origin
Continuous-flow processing	Heat and mass-transfer control; improved process safety in suitable cases	Equipment and downstream integration; clogging or pressure issues	Throughput, energy, safety and product consistency

The comparison indicates that sustainability is context-dependent. A method may be advantageous for one product and unsuitable for another. The strongest cases are those in which improved selectivity, reduced material input, lower hazard and feasible scale-up occur together.

VII. DISCUSSION

The review indicates that green chemistry is most effective when it is incorporated early in route selection and process development. Waste prevention and atom economy encourage chemists to question reaction pathways before process conditions are fixed. However, reaction-level indicators cannot capture the full burden of solvents, purification, utilities and raw-material production. Process metrics such as PMI and E-factor provide a broader view of material use, while life-cycle assessment can identify impacts outside the factory gate. Catalysis, biocatalysis and selective synthesis can create benefits beyond the reaction vessel. Better selectivity may reduce the number of purification stages and lower the need for solvents, adsorbents and energy. Likewise, solvent reduction can decrease material consumption but may create new mixing or heat-transfer requirements. This illustrates why isolated improvements should be checked against the complete process. The approaches reviewed offer complementary rather than interchangeable routes to sustainable chemical production. Safer solvent selection addresses exposure and emissions; solvent-free and mechanochemical methods target material use; catalysis and biocatalysis improve reaction efficiency and selectivity; renewable feedstocks alter the resource base; and flow or other intensified methods can improve control and safety. Combining approaches may be more effective than adopting any one in isolation. For instance, a catalytic reaction using a safer solvent in a continuous reactor may reduce waste and improve process control, provided the combined system is technically and environmentally sound.

Industrial decisions must also account for economics and supply-chain resilience. A lower-hazard solvent may cost more or require equipment changes. A renewable feedstock may be locally available but seasonally variable. A catalyst may perform well initially but lose activity after repeated cycles. These factors influence process reliability and the real cost of implementation. Economic feasibility and environmental performance should therefore be assessed together, while keeping the two forms of evidence distinct.

A further consideration is the relationship between product design and process design. The principles of green chemistry include designing products for degradation and reducing hazards throughout their life cycle. For polymers, coatings and specialty materials, product durability, repairability, recyclability and disposal can be as consequential as the synthesis route. A product that performs poorly may require more frequent replacement, offsetting gains made during manufacture.

The review suggests several priorities for future research. First, studies should report complete material inputs, solvent quantities, energy requirements, yields and waste streams using clearly stated boundaries. Second, greener alternatives should be compared with realistic industrial baselines rather than idealised conventional routes. Third, research should focus on catalyst systems that use abundant elements, remain active over multiple cycles and can be recovered safely. Fourth, renewable feedstock studies should include sourcing and land-use considerations. Finally, scale-up studies should address process safety, reproducibility and downstream operations from the outset.

VIII. CONCLUSION

Green chemistry provides a practical framework for redesigning chemical synthesis so that environmental and health concerns are addressed at the source. Recent directions in safer solvents, solvent-free and mechanochemical synthesis, catalysis, biocatalysis, renewable feedstocks, microwave-assisted methods and continuous-flow processing offer opportunities to reduce hazardous inputs, material waste and energy demand. Their industrial relevance is strongest when improved reaction performance also simplifies separation, supports consistent product quality and remains feasible at scale. The review demonstrates that no method can be considered sustainable solely because it is solvent-free, catalytic, bio-based or energy-efficient in one stage. Meaningful assessment requires complementary indicators such as atom economy, PMI and E-factor, together with hazard evaluation and, where appropriate, life-cycle assessment. Transparent boundaries and consistent reporting are essential for valid comparisons.

Future progress will depend on collaboration between synthetic chemists, chemical engineers, environmental scientists and industry. Priority areas include robust and recyclable catalysts, safer renewable feedstocks, scalable low-waste transformations, integrated process design and better environmental data. By connecting molecular design with process engineering and life-cycle thinking, green chemistry can contribute to chemical manufacturing that is more resource-efficient, safer and better aligned with long-term sustainability goals.

IX. POLICY AND INDUSTRIAL IMPLICATIONS

1. Encourage prevention-oriented process design: Research funding and industrial development programmes can reward waste prevention, safer reaction pathways and improved material efficiency rather than relying only on end-of-pipe treatment.
2. Promote consistent sustainability reporting: Academic and industrial studies should report reaction yield, solvent and reagent use, energy demand, waste generation, catalyst loading and recovery, and clearly state system boundaries.
3. Support safer chemical and solvent substitution: Institutions and manufacturers should use structured hazard and performance assessments when selecting solvents, reagents and process aids. Substitution should avoid regrettable replacements that transfer risk to another stage.
4. Strengthen scale-up and industry–academia collaboration: Pilot studies, shared facilities and process-safety expertise can help translate laboratory methods into reliable manufacturing routes. Scale-up assessments should include mixing, heat transfer, separation, equipment compatibility and worker safety.
5. Integrate life-cycle thinking into product development: Renewable feedstocks, bio-based materials and recyclable products should be evaluated across sourcing, manufacture, use and end-of-life stages. Environmental claims should be supported by transparent evidence rather than by labels alone.
6. Build capacity in green chemistry education: Chemistry curricula and laboratory training can include solvent selection, waste audits, process metrics, safer handling and critical evaluation of sustainability claims. This can prepare researchers and future industrial chemists to incorporate environmental considerations into routine decision-making.

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