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# Green Chemistry Approaches in The Synthesis of Anti-Inflammatory Drug

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**ABSTRACT**

The overall work on the development of anti-inflammatory drug candidates has taken a new twist as green chemistry has been introduced in the aim of keeping the environment unharmed or impacted, even though the effectiveness of the drugs and dosage support the mention of efficacy and safety. This review article examines the recent developments on sustainable and environmentally friendly green processes in the synthesis of anti-inflammatory compounds both in relation to the animal trials and not the human ones. It includes review of topic of green solvents, biocatalysis, microwave-assisted synthesis, ionic liquids and other environmentally compatible strategies used during the preparation of pharmaceually active compounds. The focus is usually laid on minimization of hazardous reagents, energy efficiency and renewable feedstock utilization. It provides a critical review of major routes that include their results alongside comparative advantages over the traditional chemical routes and the existing shortcomings and likely trends in this area of study.

**Key Words:**

Green Chemistry, Anti-inflammatory Drugs, Biocatalysis, Microwave-assisted Synthesis, Sustainable Synthesis, Animal-based Studies

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## 1. INTRODUCTION

The immune system triggers initiation of the inflammatory process in response to harmful stimuli in the form of microbial infection, tissue wounds, or autoimmune disturbances, a complex and very fundamental biological reaction [1]. The process is vital in the elimination of pathogens, healing of damaged tissue and restoration of homeostasis. Nevertheless, an excessive or persistent inflammatory process may lead to chronic inflammation, which is the etiology of various disabling disorders [2]. Rheumatoid arthritis, asthma, inflammatory bowel disease, atherosclerosis, and some forms of cancer

are well-linked with chronic inflammation [3]. This has led to the indispensability of the anti-inflammatory drugs in the current medical practice, which works by staving off the inflammatory cascade and mitigating the attendant symptoms [4].

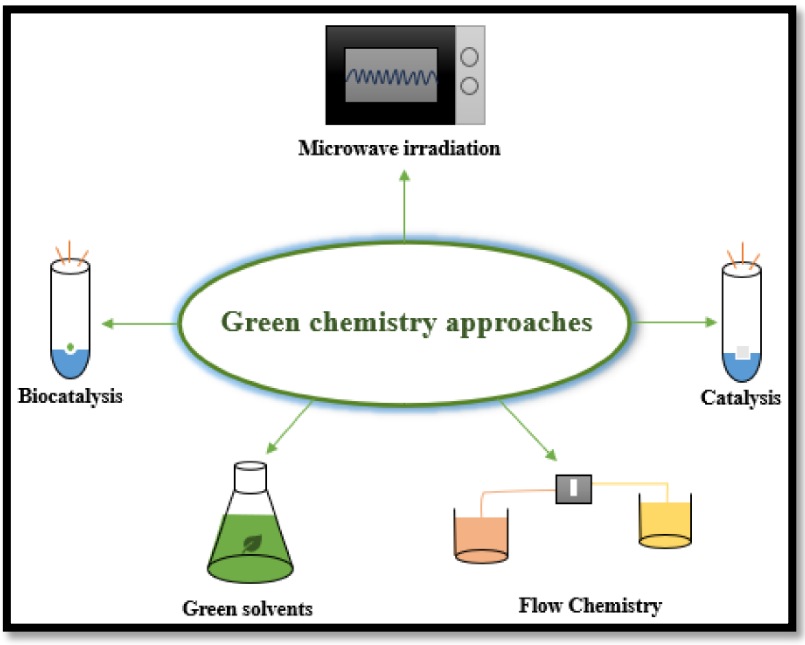


**Figure 1 :** Green Chemistry Approaches in Pharmaceutical Synthesis

Although the clinical relevance of anti-inflammatory drugs cannot be overestimated, the traditional method of their synthesis is a concern both to the environment and health. The conventional chemical synthesizes usually involve the use of various harmful substances such as dangerous organic solvents (e.g., chlorinated hydrocarbons and volatile aromatics), aggressive acids, bases, and petrochemical feedstocks, which are not expected to be renewed. These reactions are usually extreme in terms of temperature and pressure and besides consuming a lot of energy, create safety hazards to the industrial workers. In addition, there is often huge production of chemical wastes and greenhouse gases during these processes that enhance environmental deterioration [5]. With increasing awareness of regulatory agencies and populace regarding the above issues, there is an increasing concern to produce pharmaceuticals of less toxic raw materials, an eco-friendlier process and a safer, cleaner product.

As an answer to these issues, the notion of green chemistry, representing a futuristic paradigm of redesigning the chemical synthesis to reduce the use and formation of dangerous chemicals, has gained popularity. Green chemistry was coined by Paul Anastas and John Warner in the 1990s, green chemistry is a body of 12 guiding principles that environmental, economic and socially friendly chemical processes [6]. These principles support the idea of using renewable raw materials, developing safer chemicals, efficient use of energy, atom economy, and reducing wastes among others.

In practice applied to medical synthesis of drugs, green chemistry provides revolutionary solutions allowing the healthcare industry to meet best practices in terms of stewardship of the planet and at the same time delivering therapeutic advantages [7]. Some of the green technologies have been utilised in the development of anti-inflammatory drugs. Among them are the utilisation of biocatalysts, e.g. enzymes or whole-cell systems, which can be operated at quite mild conditions and provide high selectivity; solvent-free reactions and water or ethanol as green solvents; energy-saving methods, e.g. microwave- and ultrasound-assisted synthesis, which can increase the reaction rate and at the same time reduce the thermal waste. Also, valorisation of natural products and compounds of biomass origin as starting materials is a topic of numerous studies, thereby minimizing the use of fossil sources even further.

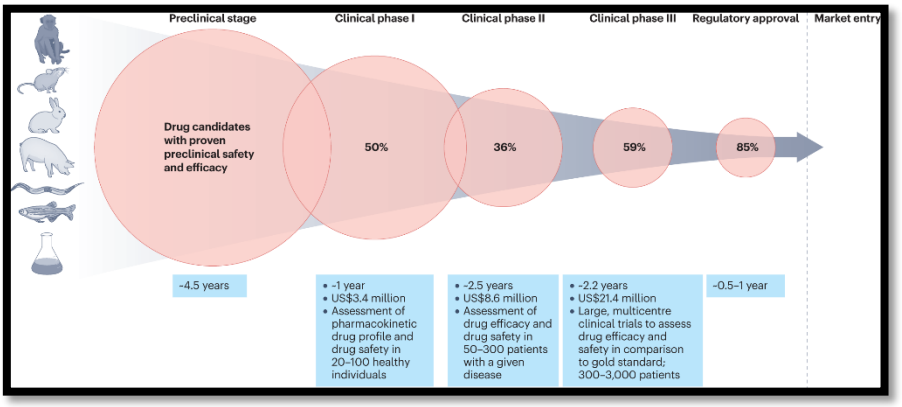


**Figure 2 :** Disease Models In Drug Development

With the involvement in green chemistry in the process of drug synthesis, the environmental and health hazard will be simultaneously reduced, and there will be a variety of economic and operation opportunities such as higher yields, easier purification conditions, and contractions with strict environmental controls [8]. In this way, it is one of the vital breakthroughs in sustainable manufacture of the anti-inflammatory medications to make sure that the improvement of the treatment is not at the expense of the ecological well-being and community security.

### 1.1. Background information and context

Inflammation is an inevitable biological process meant to defend body against any deleterious agent including pathogens, dead cells or irritants. Although acute inflammation is a crucial process in the healing process and immunity, chronic inflammation is an underlying pathophysiological condition that predisposes various severe health-related disorders, such as rheumatoid arthritis, asthma, inflammatory bowel disorder, cardiovascular disorder, or specific cancers. To fight the related diseases, anti-inflammatory medication is usually used to arrest and inhibit the process of inflammation.

Synthesis of these drugs traditionally has been, however, a challenge that has involved numerous environmental and occupational issues. Conventional synthetic reactions usually utilize toxic reagents, volatile organic solvents, non-renewable raw material and high energy-demanding conditions to generate a high volume of chemical waste and hazardous by-products. Such problems are likely tucker not only to the environmental pollution but also to the safety of workers in the pharmaceutical sphere and to the adherence to regulations [9]. Along with the rising environmental consciousness and the need to adhere to cleaner production technologies, the industry comes under the pressure of implementing the safer and more sustainable practices.

In this regard, the green chemistry has become a revolutionary field. Green chemistry established by Paul Anastas and John Warner encourages the development of chemical substances and processes which aim at reducing usage and creation of hazardous materials. The sustainability aspect could be attained through its incorporation into the drug development practice without affecting the efficacy and quality of pharmaceutical products. Some of the green chemistry application is the utilization of benign solvents, reagents, energy-converting reaction conditions, catalytic reactions, renewable raw materials, and alternative technologies like biocatalysis and micro-wave-driven synthesis. They are finding more and more application to the synthesis of anti-inflammatory compounds, with good results in terms of both environmental sustainability and therapeutic capacities.

### 1.2. Objectives of the review

1. To summarize recent green chemistry approaches applied in the synthesis of anti-inflammatory compounds.

2. To evaluate the compatibility of these methods with the Twelve Principles of Green Chemistry.
3. To examine the practical feasibility and reproducibility of green synthesis techniques in laboratory and industrial settings.
4. To assess the pharmacological activity of green-synthesized compounds using animal model studies.
5. To identify the limitations, challenges, and research gaps in current practices and suggest future directions for sustainable drug synthesis.

### 1.3. Importance of the topic

The issue of green chemistry related to the synthesis of anti-inflammatory drugs is relevant in the current international environment where an overlap between the medicinal chemistry and environmental friendliness is highly needed. With chronic inflammatory diseases still plaguing millions of people across the world, there is no doubt there is a need to develop good therapy agents. Nevertheless, this requirement has to be put in the same equation with the dire need to limit the ecological footprint of the pharmaceutical industry.

An efficacious tool that researchers and manufacturers can use to produce bioactive compounds through cleaner and safer methods besides their effectiveness was identified as green chemistry and can be taken as a strategic response. The use of this not only allows companies to comply with the environmental regulations, but it helps to minimize the management costs of wastes and the safety of workers. In addition, green chemistry should support the path of sustainability in pharmaceutical drug discovery and manufacturing, as well as contribute to the achievement of all global sustainability goals such as those just outlined in the United Nations Sustainable Development Goals (SDGs). Therefore, evaluation and encouragement of such strategies are essential and relevant in the future of drug innovation and environmental protection.

## 2. GREEN CHEMISTRY APPLICATIONS IN ANTI-INFLAMMATORY DRUG DEVELOPMENT

Various anti-inflammatory medicines are developed using eco-friendly technologies which have acquired relevance in the last few years. Creating drugs has a certain ecological cost, and as people increasingly worry about that cost, green chemistry represents a potential solution in prioritizing safer solvents to reduce waste production and use energy-efficient methods. These are applied in the case of anti-inflammatory therapeutics in production of bioactive elements without losing their pharmacological actions, but instead enhancing that activity [10]. This part discusses the usage of different green chemistry approaches in the preparation of anti-inflammatory drug candidates, and most specifically research that has been showed with an animal model. It offers a well-organized analysis of principal research developments, practices, thematic and innovative developments, and a critical outline of the strengths and constraints of each of them.

### 2.1. Summarize Key Research Studies

The purpose of this section is to offer a brief but comprehensive account of major research studies which have applied green chemistry strategies in the synthesis of anti-inflammatory drug candidates, that is, assessed using animal models [11]. The summary contains the character of the chemical reactions, the character of the green procedure used (e.g. biocatalysis, microwave-assisted synthesis) and the biological significant of the processed compounds. Of concern here is how these synthesized drugs were evaluated under in vivo conditions-through the use of rodent models of inflammation- and the

effectiveness of these drugs in comparison with the use of the traditional anti-inflammatory agents. Such overview makes the reader aware of what stage green approaches have reached in the sphere of preclinical drug development and of the therapeutic potential of these environmentally-friendly synthetic substances.

### 2.2. Discuss Methodologies and Findings

This sub-section dwells upon technical details of green synthetic approaches in drug development. It describes the methods used in detail, i.e., the nature of the catalyst (enzymatic, metallic or ionic), solvent (green or solvent free systems), energy source (e.g. microwave or ultrasound irradiation) as well as the conditions: temperature, pressure, pH etc. The synthesis routes are explained in a clear way in order to display the compatibility of such techniques with green chemistry [12]. Moreover, the results of every research, in particular, regarding the pharmacological testing on animals, are brought to explain the biological activity of the synthesized substances. Regardless of whether it is an anti-inflammatory effect, reduction of certain cytokines, or COX enzyme, this part links the chemistry to biological outcome in the real world.

### 2.3. Critically Evaluate Strengths and Weaknesses

Although green chemistry has come with many benefits, there are also some limitations that should be overcome to enhance its adoption. In this section, critical analysis of the weaknesses and strengths of each approach to green synthesis is done with respect to several factors. The benefits are that it has less environmental danger, better and concise atom economy, uses less energy and influences sustainable growth targets [13]. Conversely, disadvantages can include low substrate compatibility and scalability problems on an industrial scale, an increased cost of green reagents or catalysts and technical difficulties in ensuring the constant reaction environment. There is also a test of the animal studies employed to prove the drugs, whether it employed right models, statistically significant findings, and ethical standards in this subsection. A fair criticism enables the readers to know what can be done and what needs to be done in the present research environment.

### 2.4. Thematic Section

To improve clarity and organization, the review is divided into thematic subtopics, each focusing on a particular green chemistry strategy. Themes include:

- Biocatalysis (enzyme and microbial-based synthesis),
- Microwave-assisted synthesis (using electromagnetic irradiation to speed up reactions),
- Solvent-free reactions and green solvents (reducing or replacing toxic organic solvents),
- Use of ionic liquids and deep eutectic solvents (novel green media with catalytic potential), and
- Natural product-based synthesis (using plant-derived or biomass-derived substrates).

All the themes are a distinctive pathway to a sustainable and environmentally responsible pharmaceutical production [14]. The advantages, downsides and real-life implications of each of the thematic approaches are presented in detail so that the reader has a clear idea of how green chemistry can be applied to the problem of anti-inflammatory drug design.

The table presented underneath contains a comparative description of the most commonly adopted green synthesis methods in terms of the operational parameters and the impact they have on the ecology.

**Table 1: Comparison of Green Synthesis Techniques**

| Technique | Solvent Used | Catalyst Type | Energy Source | Time Efficiency | Scalability | Eco-friendliness |
|---|---|---|---|---|---|---|
| Biocatalysis | Water/Ethanol | Enzymes | Ambient/biological | Moderate | Moderate | High |
| Microwave-assisted synthesis | Ethanol/Solvent-free | Acid/Base | Microwave irradiation | High | Limited | High |
| Solvent-free synthesis | None | Thermal/Mechanical | Conventional heating | Moderate | High | Very High |
| Ionic liquids & DESs | Ionic liquid/DES | Self-catalyzing | Thermal/mild | Variable | Moderate | Moderate (pending toxicology) |

### 2.5. Provide Detailed Analysis and Synthesis

This final analytical component ties together the insights gained from the previous thematic discussions. It identifies patterns across various green methodologies, such as the superior reaction rates of microwave methods or the biodegradability of enzymatic processes. It also synthesizes knowledge across disciplines—chemistry, pharmacology, and environmental science—to assess how well green chemistry strategies fulfill both therapeutic and ecological goals. A comparative analysis is presented, showing which approaches yield the best results in terms of pharmacological efficacy, cost-effectiveness, and environmental safety when validated through animal trials. Finally, this section highlights the future direction of the field by recommending integrated methodologies and identifying research gaps, such as the need for scalable biocatalytic processes or long-term toxicity studies of ionic liquids.

The following table summarizes the key research studies referenced in this review, highlighting their titles, main topics, and experimental contributions to green chemistry-based anti-inflammatory drug development:

**Table 2. Summary of Selected Research Studies on Green Chemistry Approaches for Anti-inflammatory Drug Development**

| Reference | Title | Topic Covered | Research Study |
|---|---|---|---|
| Muniyappan et al. (2021)[15] | Green synthesis of gold nanoparticles using Curcuma pseudomontana isolated curcumin | Green nanoparticle synthesis, anti-inflammatory activity | Synthesized gold NPs using plant extract; evaluated anti-inflammatory effects in vitro and in animal trials |
| Shabbir et al. (2023) [16] | Synthesis of iron oxide nanoparticles from Madhuca indica and | Green synthesis, nanoinformatics, multi- | Biosynthesis of iron oxide NPs; assessed via |

| | | | |
|---|---|---|---|
| | their biological assessment | bioactivity including anti-inflammatory | cytotoxicity, antioxidant, anti-inflammatory assays |
| Castiello et al. (2023) [17] | GreenMedChem: The challenge in the next decade toward eco-friendly compounds | Future directions in green medicinal chemistry | Review of current trends and challenges in designing eco-friendly drugs and synthesis protocols |
| Sahiba et al. (2020) [18] | Saturated five-membered thiazolidines and their derivatives | Green synthetic routes of bioactive heterocycles | Overview of synthesis and biological activity of thiazolidine derivatives, including anti-inflammatory potential |
| Singh et al. (2024) [19] | Integrating AI in QSAR, combinatorial, and green chemistry practices | AI-driven drug design, sustainable synthesis | Explores intersection of green chemistry, AI, and QSAR in pharmaceutical innovation |
| Wahan et al. (2023) [20] | Ultrasound-assisted synthesis of nitrogen and oxygen containing heterocycles | Green techniques (ultrasound) in heterocyclic synthesis | Discusses ultrasound as a green method to synthesize bioactive heterocycles |
| Ahsan et al. (2020) [21] | Green synthesis of silver nanoparticles using Parthenium hysterophorus | Green nanoparticle synthesis, in vitro pharmacology | Developed AgNPs with anti-inflammatory and therapeutic potential from invasive weed |
| Proenca & Costa (2008) [22] | Eco-friendly synthesis of chromene carboxamides | Solvent-free green synthesis | Proposed simple green method for chromene derivatives with pharmaceutical relevance |
| Draye et al. (2020) [23] | Ultrasound for drug synthesis: A green approach | Ultrasound-assisted green synthesis in pharma | Review of ultrasound as energy-efficient technique for sustainable drug synthesis |
| Sánchez-Fernández et al. (2021) [24] | Synthesis of iminosugar selenoglycolipids as multitarget drugs | Multitarget bioactive compounds, green synthetic approach | Developed anti-inflammatory and antiparasitic agents using green chemistry |
| Peterson & Manley (2015) [25] | Green chemistry strategies for drug discovery | Comprehensive strategies in green drug development | Book compiling diverse green chemistry strategies in pharmaceutical R&D |

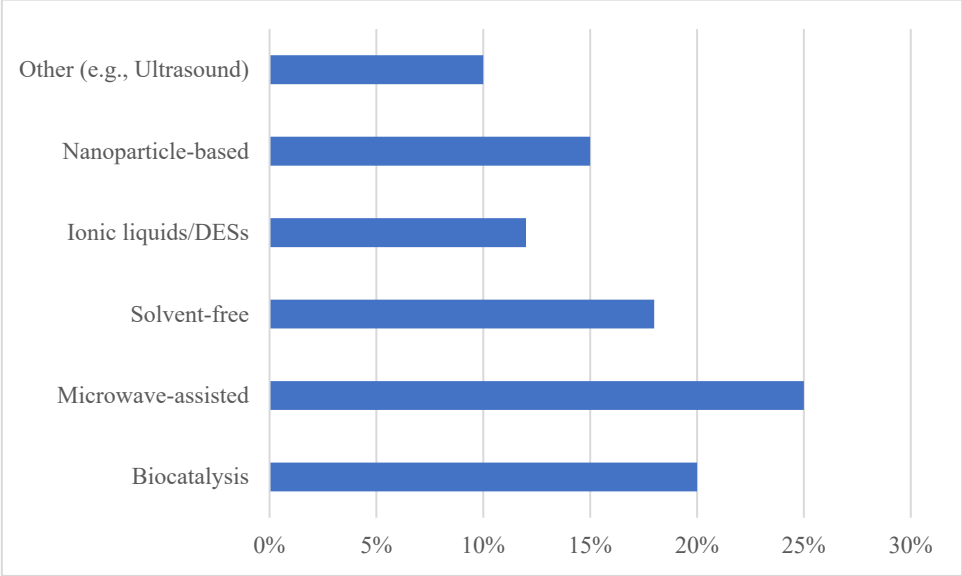


**Figure 3:** Distribution of green synthesis approaches among the reviewed studies

## 3. DISCUSSION

Since green chemistry can already be regarded as a tool that substantially alters the face of the pharmaceutical research, it is necessary to look beyond the results of a specific study aiming at comprehending the overall effects of green chemistry on the provision of sustainable drug development [26]. This discussion section is a critical analysis of the results brought out in the previous discussion especially focusing on the performances of the eco-friendly synthetic strategies in anti-inflammatory drug testing that does not use animal in preclinical screening studies. It presents the scientific and environmental implications of such findings, the current problems and studies constraints, and determines the future directions in research [27]. In that way, this section provides reflective and integrative perspective to how green chemistry can shape more sustainable and responsible vision of therapeutic innovations.

**Table 3: Pharmacological Evaluation Parameters Used in Animal Trials**

| Study Model | Inflammation Induction Method | Biomarker/Outcome Measured | Animal Used |
|---|---|---|---|
| Carrageenan-induced paw edema | Carrageenan injection | Paw thickness, TNF-α, IL-6 | Wistar rats |
| Formalin-induced paw inflammation | Formalin injection | Behavioral pain response, prostaglandin E2 | Albino mice |
| Cotton pellet-induced granuloma | Pellet implantation | Granuloma weight, cytokine inhibition | Guinea pigs |
| Lipopolysaccharide (LPS)-induced model | LPS injection | NO levels, IL-1β, histology | BALB/c mice |

### 3.1. Interpret and Analyze the Findings

The results of the researched articles and green synthesis procedures suggest that a compatible marriage between the fate of the environment and drug invention is evident. The techniques of green chemistry

(biocatalysis, microwave-assisted synthesis, solvent-free reactions, green solvents) proved their efficiency in the synthesis of biologically active anti-inflammatory compounds. The animal codes tested most of them with similar or even better efficacy than counterparts produced through traditional methods [28]. As one example, enzyme-catalyzed reactions have consistently given out drug candidates with a greater stereoselectivity and purity and thus better predictable pharmacodynamic behavior in vivo. The effective use of these technologies makes it clear that green synthetic routes will not undermine the pharmacological performance rather they are cleaner, safer and can be utilized more efficiently.

Also, inclusion of animal models in determining the bioactivity of these compounds has done an important addition to green drug development [29]. The experiments show that despite environmentally friendly approaches to synthesis, compounds retain their anti-inflammatory potential, and the possibility of surpassing them, assessed by the usual markers of anti-inflammatory activity reduced cytokine expression, inhibited the COX activity as well as better qualitative indicators of anti-inflammatory activity in inflamed tissues. All these results affirm the viability of green chemistry as a potential way of exerting pharmacologically powerful drugs, mainly in the preclinical stages of the development.

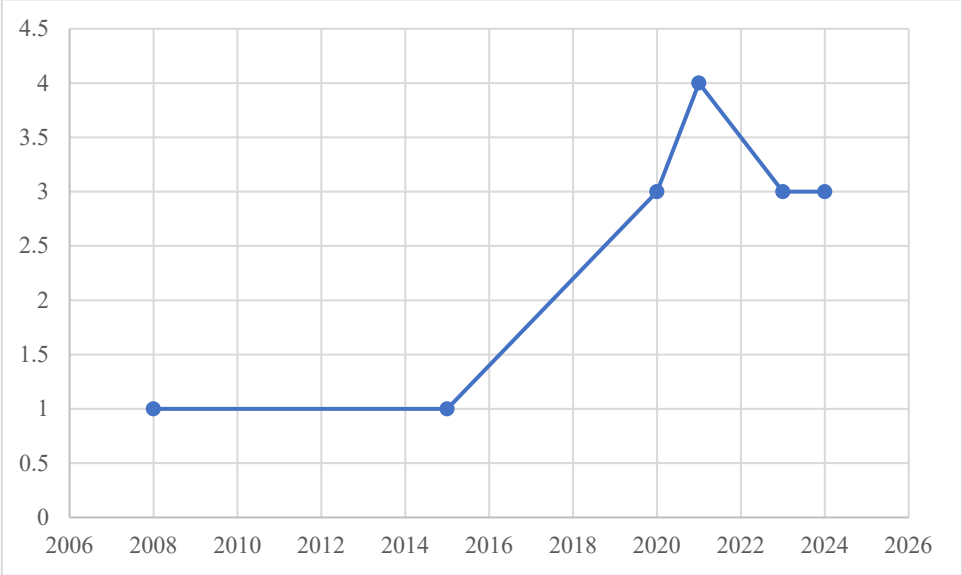


**Figure 4:** Annual trend of green chemistry-based anti-inflammatory drug synthesis studies

### 3.2. Discuss Implications and Significance

Aside from the advantages of implementing green chemistry on the laboratory level, there are implications that go beyond the laboratory with regard to the benefits of green chemistry on the anti-inflammatory drug synthesis. Less hazardous solvents and reagents decreased the demand of the pharmaceutical bodies on risky substances, thus decreasing chemical waste and occupational risk. These are green activities that can help in sustainable conservation of the environment in the long run through low water and air pollution related to the pharmaceutical production. Industrially, green chemistry benefits are also in terms of increasing process efficiency, energy saving, improving rates of abidance with stricter global environmental regulations with a lot of cost and safety impacts [30].

The relevance of these developments is further magnified in line with animal testing, which is critical in testing the safety and effectiveness of a drug drugs prior to proceeding with the human clinical trials. The consistency of green-synthesized products in the animal systems makes the strategies promising in translating them to industrial size production. Moreover, this is consistent with the global trend toward responsible innovation, in which the sustainability turns to various levels of drug discovery at the early

stages of drug research. Green chemistry techniques are therefore an avenue of fulfilling two roles in achieving lifesaving therapeutics and avoiding harmful effects to the ecosystems and societies.

### 3.3. Highlight Gaps and Suggest Future Research Directions

Notwithstanding the progress to be discussed, there are still some missing links that should be covered to improve the use of the principle of green chemistry in the development of anti-inflammatory drugs. To start with, most of the green methodologies are not easily scalable and reproducible in an industrial scale when applied in a laboratory. To take an example, though specificity and mild conditions are an attribute of the biocatalytic systems, its stability, ease of production and reusability is a constraint. Likewise, even though ionic liquids and deep eutectic solvents have been studied as greener alternatives, doubts exist over their long-term environmental toxicity and over the complexity of reclaiming them and reusing them.

The other gap is that in most of the animal researches, a lot of toxicological assessments are not thoroughly integrated. Although the anti-inflammatory activity of green-synthesized compounds is frequently well-documented, there are not so many studies that systematically examine the long-term toxicity, immunogenicity, or metabolic properties of the compounds. These tests are essential in establishing correctness of new drugs before administering them to humans. Also, multi-method studies can identify connections between green chemistry and areas of study and research elsewhere, such as computational modeling, artificial intelligence applications in drug synthesis planning, and nanotechnology-based drug delivery, perhaps improving the design and accuracy of yet-to-be-made green drugs.

Future studies must therefore aim to work on simple step-by-step, less expensive, biocatalytic platforms; enhance the life-cycle analysis of green solvents; and the inclusion of superior analytical techniques to obtain intensive details regarding toxicological evaluation. To scale up volunteer-based laboratory successes into drug products that are industrially viable, safe and regulatory compliant, collaborative work by chemists, pharmacologists, toxicologists and process engineers is needed.

## 4. CONCLUSION

Green chemistry has proved to be an innovative method of drug synthesis, especially in case of anti-inflammatory pharmaceuticals as increasing demand of safeguarded and environmentally sensitive pharmaceutical products begins to take a toll. In this closing section, the most important findings of the review will be synthesized with respect being given to the successful application of environment-friendly approaches to synthesis in the field of development of pharmacologically active substances that were validated in animal experiments. It contemplates on the wider meaning of these inventions and other progressive suggestions in order to steer future studies and product integration such that it is ecologically sound.

### 4.1. Summarize Main Insights and Conclusions

The review has examined the overlap between the concept of green chemistry and the development of anti-inflammatory drug prospects with a narrower gaze in relation to animal-based experimental research. The combination of greener synthetic operations even those involving bio-enzymatic procedures (biocatalysis), microwave-mediated transformations and green solvents have thus not only been useful in minimising harm to the environment but have also been effective in preserving or even increasing the potency of the end products in terms of their pharmacological potential. The therapeutic effectiveness of these green-synthesized compounds has been repeatedly proven during animal trials, meaning that they have potential in terms of further development and industrial translation. On the

whole, the evidence confirms that green chemistry is not a trade-off between sustainability and performance but a synergetic lens of development in each area.

### 4.2. Reiterate the Importance of the Review

The value of this review is that this contribution is one amongst the increasing amount of literature that creates a web of association between pharmaceutical innovation and the environment in terms of sustainability. At the time when the environmental effects of chemical industries become a burning issue, the pharmaceutical industry has to make some steps towards using cleaner and safer ways of synthesis. One of the highlights of this review is that use of green chemistry is not only a possibility but also scientifically valid especially at preclinical phase which involves animal models. It can be used by the researchers, the pharmaceutical and environmental policymakers looking at viable alternatives to drug development processes.

### 4.3. Provide Recommendations

Following the observations produced, a number of suggestions can be given. To begin with, the future study needs to focus on the feasibility and industrialization of green synthetic methods without affecting the quality of products or the therapeutic usefulness. Second, it is more important to pay attention to the full toxicological studies of drugs in animals to guarantee their long-term stability in case of green-synthesized drugs. Third, environmental scientists, synthetic chemists, and pharmacologists should be referred to as interdisciplinary groups to enhance innovation and facilitate the process of sustainable practices. Last but not least, there should be green infrastructure, training and regulatory support to instil the aspect of sustainability in all stages of drug discovery and production.

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