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A Review on Green Chemistry and Its Applications

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ABSTRACT

Green Chemistry is most investigated subject these days. It is also known as sustainable chemistry. Green Chemistry and sustainable chemistry are equals that helps to save and conserve resources. It decreases the effect of chemical products on human and atmospheric health. Green Chemistry gives 12 principles that reduce and prevent the utilization and manufacture of hazardous substance. These principles of green chemistry inform about the various issues related to production of chemical compound. Green Chemistry concept started approximately three decades ago. Green chemistry concept for the chemical synthesis and application launched in 1990. This review article purpose to study about Green chemistry and its application and how green chemistry connect to the phytochemistry.

By establishing Green Aspiration Level (GAL) that is a quantifiable descriptor, process greenness becomes measurable. Green house gases and global warming are the problem that affected the human and environment health. Green chemistry is used in daily life mainly in medicines. Tree bark and Pine bark extracts are mostly used in anti-microbial, antioxidant and anticancer drugs. The matter that present in environment gives applicable things to the researchers and engineers for the changing and developing a sustainable culture. The word "Green chemistry" is given by the IUPAC which means: the invention, design and utilization of chemical product and process to reduce or to eliminate the use and production of unsafe substance.

KEYWORDS: Green chemistry, Green chemistry in Pharma Industry, Principles of Green chemistry, Circular economy.

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INTRODUCTION

Green chemistry is related to the environment, which mainly focus on the development of a new chemical/ product that reduce and prevent the environmental toxicity. Anastas and warner give 12th principles of Green chemistry in 1990s. The growth of sources that prevent the depletion of natural resources has compromise with many ways, such as uses of Green chemistry principles [1, 2].

Many chemical industries mainly pharmaceuticals encounter critical environmental issue from many years. Most of the chemicals products synthesis having a large scope but these compound produce hazardous wastes such as a organic compound Phloroglucinol that is used in the synthesis of pharmaceuticals and explosive, Phloroglucinol produce a large amount of solid waste [3].

'Silent Spring' a scientific book which published in 1960s tells about how natural source are misused and how chemical damaged the environment. In 1970s Environmental Protection Agency or EPA was begin. A conference in Sweden in 1972s, named 'Stockholm conference' in which members of the United States was participate and talk about the environmental shrinkage and depilation in ecosystem. After developing EPA, chemical industries and researchers are sensible for the environmental pollution until 1980s. A special authority OECD (The Organization for Economic Co-operation and development) spread around 30 countries conducted a meeting for the change in synthesis of existed chemical during synthesis process, after that Anastas publish a paper in which 12th principle of green chemistry was given [4, 5] .

PRINCIPLES OF GREEN CHEMISTRY:

Paul Anastas and John Warner give 12th principle of green chemistry, Green chemistry draw chemical which are not harm to the environment and reduce hazardous substance from environment [1,19]. According to the US environmental law "The Pollution Prevention ACT of 1990," designing industrial operations to avoid producing waste is the first step towards reducing pollution [1].

There are following principle of green chemistry mention in table 1.

Table 1: Principle of Green chemistry

1. Prevention	**2.** Atom Economy	3. Less Hazardous Chemical Synthesis	4. Designing Safer Chemical
5. Safer Solvents & Auxiliaries	6. Design For Energy Efficincy	7. Use Of Renewable Feedstocks	8. Reduce Derivatives
9. Catalysis	10. Design For Degradation	11. Real Time Analysis For Pollution Prevention	12. Inherently Safer Chemistry For Accident Prevention

GREEN CHEMISTRY's PLACE IN THE PHARMACEUTICAL SECTOR:

The capacity to foster or sustain a process over time without jeopardising the requirements of coming generations is known as sustainability. The design of chemical products and procedures that reduce or eliminate the usage and manufacture of hazardous compounds is referred to as "sustainable chemistry" [6]. The medical and health care sectors are expanding quickly and improvingly thanks in part to the fast development of the pharmaceutical and other industries. A new area of chemistry that uses ecological methods; it involves cutting back on or completely doing away with the usage of dangerous materials in chemical reactions, as well as lowering the amount of hazardous and toxic intermediates and products [5].

'Silent Spring', a book published in the 1960s, opened many people's eyes. The scholarly publication increased awareness of ecological perception and highlighted the dangers of excessive reliance on natural resources. The book explained how our ecology is being impacted by specific substances. In 1970, the Environmental Protection Agency (EPA) was established. The United Nations members were present at the Stockholm conference, which was held in Sweden in 1972 and was attended by numerous other nations [5, 7]. The participants in this conference talked about the environmental harms that lead to ecosystem depletion and made everyone aware of them. The EPA and the chemical industry focused mostly on pollution and dangerous substances up until the 1980s. Nonetheless, chemists saw a big change when scientists began raising environmental consciousness and looking at ways to stop pollution [7]. An international organisation made up of roughly thirty developed nations, the Organisation for Economic Co-operation and Development (OECD), convened meetings and issued recommendations centred on preventing pollution and implementing cooperative changes to current chemical synthesis processes [5, 7].

Particles with a size range of 10 to 1000 nm are known as nanoparticles. The enormous surface area of nanoparticles gives them improved properties. The real process for creating nanoparticles is environmentally dangerous and poisonous. The disadvantage of the conventional synthesis procedure is that byproducts cause contamination of the colloidal solution. Therefore, green nanoparticle production was developed to address this problem [5, 8]. These nanoparticles may be used for large-scale production and are both affordable and environmentally beneficial. This adheres to some green chemistry concepts, including prevention, the synthesis of less hazardous compounds, the design of safer chemicals, and the real-time prevention of pollution. Nanotechnology is still in its infancy in the pharmacy industry. Green production of nanoparticles is used to create bandages that promote wound healing. Next, the bandages are impregnated with the nanoparticles [5].

Drugs are manufactured using environmentally friendly methods to avoid releasing poisonous and hazardous byproducts into the surrounding environment. Nearly every green chemistry principle has been used for the same.

- The medicine sertraline is an antidepressant. Pfizer introduced sertraline to the market in 1991. Its pharmacological action is demonstrated by its inhibition of serotonin absorption.
- Another name for Talampanel is LY300164. This medication is used to treat neurological conditions such epilepsy, Parkinson's disease, and Alzheimer's disease. It targets the AMPA component in order to demonstrate its pharmacological activity.
- As a phosphodiesterase inhibitor, sildenafil works pharmacologically by preventing the phosphodiesterase enzyme from functioning. Pfizer created the product. It is mostly used for male impotence or erectile dysfunction.
- Quinapril is classified as an anti-hypertensive medication. It is used to treat congestive heart failure and hypertension, which lowers blood pressure [5].

EVALUATING THE APPLICATION OF GREEN CHEMISTRY IN THE INDIAN PHARMACEUTICAL SUPPLY CHAIN:

The production of a large portion of the active pharmaceutical ingredients (APIs) used in both generic and branded medications is currently dependent on the pharmaceutical supply chains in China and India. Nearly two-thirds of the world's APIs are produced in China, however, research indicates that Indian pharmaceutical companies are more adept at developing formulations, producing completed drugs, and promoting their products in regulated markets like the US and Europe. With revenue growth of 12% annually, the Indian pharmaceutical business is producing 20% of the world's generics, second only to China. By 2022, generics are expected to account for 92% of all pharmaceuticals sold worldwide due to increased efforts to lower healthcare costs . India is in a good position to profit from this trend; in the first half of 2017 alone, 40% of US approvals for generic medications went to Indian pharmaceutical companies, up from 35% in 2016 [8].

Since its launch in the early 1990s, GC has experienced rapid expansion due to a variety of internal and external factors, including the need to reduce environmental releases from manufacturing, pressure from stakeholders, cost savings, enhanced market positioning, improved reputation, and the capacity to draw and retain talent. Sales in the pharmaceutical sector worldwide were $996 billion in 2017 and are expected to reach $1.12 trillion by 2022. Over the coming years, pharmaceutical sales are predicted to increase at a rate of 6.3% yearly due to an ageing population and rising healthcare costs worldwide. With 45% of the worldwide prescription drug industry, the United States continues to be the world's largest market. Drug manufacturing-related environmental contamination is still a big issue and a big danger for the Indian pharmaceutical industry and "big pharma" outsourcing to India together [8].

India has had a long history of environmental pollution. It is home to one of the world's worst industrial accidents the Bhopal explosion at the Union Carbide plant in 1984, which resulted in the death toll of between 3,800 and 16,000 people. India's capital, Delhi, has been named the world's most polluted city, and a recent study discovered that the country's rivers went from 121 to 275 filthy in just five years. The discharge of untreated sewage and industrial waste has resulted in the contamination of around 80% of India's surface waters. India's Environment Ministry has designated pharmaceutical production as a "red category" because of the toxic waste it generates. The growing environmental pollution crisis in Hyderabad and Visakhaptanam, India's pharmaceutical hubs, has been documented in recent studies. A 2007 study conducted in Sweden on the effluent from a wastewater treatment plant that supplies 90 bulk medicine factories in the Hyderabad area revealed antibiotic concentrations, such as ciprofloxacin, that were more than 1,000 times more hazardous to some bacteria. Indian businesses have been found to breach quality standards, including the Good Manufacturing Practices (GMP) rules, in addition to environmental issues. The Food and Drug Administration (FDA) of the United States has increased the number of its inspections in nations producing generic medications, especially China and India, due to the growing outsourcing of drug manufacture [8].

The pharmaceutical industry generated between 25 and 100 kg of waste per kilogramme of API, more than any other sector of the chemical industry. By comparison, bulk chemicals generated less than 15 kg of waste per kg of product, and fine chemicals generated between 5 and 50 kg of waste per kg of product. This information was first reported by Sheldon. Since then, the environmental factor, often known as the E-factor, has emerged as a crucial tool for monitoring the pharmaceutical industry's efficiency and environmental gains. "The search for benign synthetic processes that reduce the environmental burden within the context of enabling the delivery of our current standard of living," is how Tucker describes pharmaceutical green chemistry [8].

The International Consortium for Innovation's Green Chemistry Working a Group is tasked with advancing green chemistry in the pharmaceutical sector & Quality in Pharmaceutical Development (IQ), a group with 32 members that was founded in 2010. After analysing the variables that go into creating a successful GC programme, created a framework with seven essential components that are needed to put the programme into action such as:

1. Teams focused on green chemistry that have the backing of management.
2. Metrics and targets.
3. Education.
4. Awareness and recognition.
5. Investment in green technology.
6. External collaborations [8].

THE RELATIONSHIP BETWEEN THE CIRCULAR ECONOMY AND GREEN CHEMISTRY:

It is becoming more and more obvious that green chemistry, by permitting the continuous sustainable cycle of resources up to the disposal, is essential to the transition from linear to circular product and material usage. Green chemistry modifies and streamlines product manufacturing processes to prevent and reduce waste, which can be seen as a method to progress towards the circular economy. A lot of effort has gone into creating synthetic processes that can be in line with the 12 GC guiding principles, with the goal of going one step further and incorporating circularity notions. Using chemicals derived from materials typically regarded as waste and extending the useful life of resources are two examples of how to lessen reliance on finite non-renewable resources. Durable raw materials are essential for the effective application of circularity so, chemical advancements are needed to lengthen a product's useful life for reuse, recycling, and use [7].

In the end, green chemistry serves as the cornerstone of a circular economy that is secure and sustainable. Green chemistry and the circular economy share the belief that materials, products, and processes should be rethought. These ideas can be combined to create a value chain and business model that outlines all of the steps involved in producing a good or service. Because GC focuses on chemical synthesis for the creation of novel materials and products, it can be crucial in ensuring circularity in two crucial sustainability factors Such as:

1. Creating chemicals and chemical processes that are safer and less harmful.
2. Using sustainable feedstocks [7].

More importantly, by laying the groundwork for innovative products that use renewable feedstocks, are designed to be reused, recycled, or recovered, and require little energy to operates, sustainable green chemistry may hold the key to unlocking the circular economy's economic potential in waste management and new product design. In order to highlight the connection between green chemistry and the circular economy and to illustrate that green chemistry may be seen as an essential tool for the shift to a circular economy and a bioeconomy, the aforementioned topics will be examined in greater detail. A schematic illustration of a system that can combine the Green Chemistry and Circular economy in a strategic sustainability framework is shown in Figure 1 [7].

The annual worldwide garbage is expected to rise from 2.01 billion tonnes in 2016 to 3.4 billion tonnes over the next 30 years. In previous decades, there was no concern about the careless disposal of materials or products that were no longer needed because natural resources seemed to be boundless [7].

Beyond lab research, GC is a commonly used technology in the industry for waste elimination at the production stage. The Green Chemistry technique has had positive outcomes, as evidenced by multiple instances, such as;

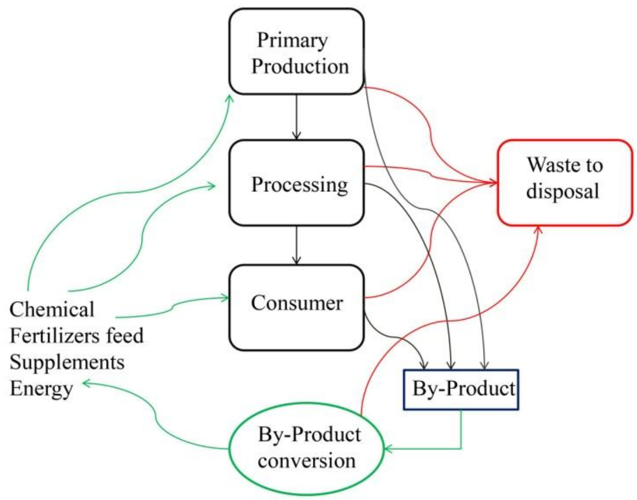

Figure 1 Schematic representation of a system that can integrate the circular economy and green chemistry in a strategic sustainability framework.

- Solvent-free paints and lacquers are already being produced by the varnish and paint industry.
- Every detergent that contained phosphorus has been phased out by the detractor industry.
- The Warner Babcock Institute for Green Chemistry has developed a non-toxic, vegetable-based hair dye named "Hairprint" as a substitute for the toxic, irritant to skin, and carcinogenic colours.
- Businesses like Merck, BMS, and Solutia have shown how safer chemicals or processes have helped them achieve more sustainable production, which reduces waste generation but also has the potential to increase synthetic product yields.
- Elevance Renewable Sciences has developed another potent, environmentally friendly degreasing solvent, Elevance CleanTM 1200, which is a bio-based solvent that does not include volatile organic compounds (VOCs). Elevance CleanTM 1200 took home the 2015 WBM Bio Business Awards' bio-based product innovation of the year award for its outstanding cleaning capabilities [7].

RELATIONSHIP BETWEEN GREEN CHEMISTRY AND THE PHYTOCHEMISTRY COMMUNITY:

Chemistry has produced a large number of useful goods with exceptional capabilities. Nevertheless, because environmental factors and criteria pertaining to the intended functionality have not been taken into consideration, this advancement has been made using reductionist definitions of both function and performance. Because of the global growth of the chemical industry, the amount of polluting chemicals that contaminate water, air, and soil has increased since the middle of the 20th century [10].

Tree bark is a forest remnant that is not widely used. It contains cellulose, hemicellulose, lignin, and other extractives such tannin, suberin, terpenoids, starch, and sugars. Bark from trees has been used for a variety of purposes since ancient times. For instance, the bark of the Himalayan Birch (Betula utilis D. Don) was employed as writing paper for Sanskrit scriptures and literature millennia ago. Bark-derived resins were used by the Egyptians to coat mummies' coffins (Austin 1994), and the Asians used bark extract from Red Sanders (Pterocarpus santalinus L.) to treat tumours and urethral discharges [11]. It is regarded as a possible resource for pharmaceutical companies and biorefineries, because tree bark contains a range of valuable compounds. Understanding these chemical components would be very beneficial for the creation of various green products with effective conversion methods [11].

There is different bark that is utilized in Pharmaceutical.

- Triterpenes (betulin, betulinic aldehyde, and b-sitosterol) found in abundance in the bark of the Plane Tree (Platanusacerifolia (Aiton) Willd) are utilised as an inhibitor of cancer cell replication.
- The human immunodeficiency virus is inhibited by betulinic acid, which is readily converted from betulin.
- The bark of Norway spruce (Picea abies L. H. Karst.) and Scots pine (Pinus sylvestris L.), two types of Nordic trees and an extract from Downey birch (Betula pubescens Ehrh. Spach) demonstrated anthelmintic

activity against Teladorsagia circumcincta, an infectious worm that infects cattle.

- Black plum bark (Vitex doniana Sweet) extract is used in Nigeria to make medicinal soap that targets the skin-infecting bacteria Staphylococcus aureus. It possesses both antibacterial and antifungal properties.
- By lowering oxidative stress, the extract from the bark of red pine (Pinus brutia Ten) protects chromatin damage and improves bull sperm quality [11].

Tree bark extracts are used as natural dyes since they are low toxicity, biodegradable, and cause little adverse reactions. The Brazilian native Croton urucurana Baill has tannin, which has been shown to have the potential to be a natural dye with color-fastness qualities for textile dyeing. The bark of walnut trees (Juglans regia L.) stains woollen yarn well, producing a range of pale to bright greyish to yellowish-brown hues with different depths [11].

Numerous microorganisms create lactic acid, an organic acid with a wide range of uses in the food, chemical, pharmaceutical, and polymer industries. The market for lactic acid has expanded gradually as new, eco-friendly products have been released. Thus, a key area of research focus is the development of novel technologies for lactic acid production that have higher yields and lower production costs [14]. Scheele made the discovery of lactic acid in acid milk in 1780. Both chemical synthesis and biological manufacturing methods are used in the commercial manufacture of lactic acid [12].

I. **Chemical synthesis-** Lactic acid is a by-product of acrylonitrile technology and can be produced by the lactonitrile pathway, which Wislicenus developed in 1863. The original method of making lactonitrile was adding hydrogen cyanide to liquid acetaldehyde while it was under high pressure and in the presence of a basic catalyst. After that, methyl lactate was created via esterification with methanol and hydrolysis with sulfuric acid. Ultimately, distillation was used to separate the methanol and recover the pure lactic acid [12].

II. **Biological Synthesis-** The method of biologically synthesizing lactic acid typically involves two steps: the first step is Lactic acid fermentation and the second step is product recovery and/or purification. Currently, fermentation produces around 90% of the lactic acid [12].

OVERCOMING PHARMACEUTICAL INDUSTRY BARRIERS TO GREEN CHEMISTRY:

In the 1990s, the idea of "green chemistry" was presented for use in chemical research, development, and operations [1, 19]. Noyori said it so beautifully: Green chemistry is more than just a buzzword. This fundamental tenet of chemical research is essential to the survival of our civilised society in the twenty-first century and beyond. The scientific community still has a long way to go before fully adopting green chemistry due to a number of issues, including organizational, financial, legal, technical, and cultural limitations [13].

There are obstacles unique to the pharmaceutical sector. As a drug advances through development, any modification to the synthesis process for an Active Pharmaceutical Ingredient (API) becomes more difficult due to the growing regulatory requirements at each stage of the process. Additionally, changes made closer to the end of the manufacturing process have a greater potential impact on the quality of the API [13].

There are some Green Chemistry Barriers in the Pharmaceutical Industry:

- Brief Cycle of Development.
- Restricted Duration of Patent.
- Product Excellence.
- Regulations Needed.
- Absence of Common Measures.
- High Development Cost.
- Elevated Project Attrition Rate.

APPLICATION OF GREEN CHEMISTRY IN PHARMA INDUSTRY:

A. **Biomass Utilization-**

All molecular and macromolecular chemicals derived from vegetables, forestry products, agriculture, and anything leftover are referred to as biomass. Utilizing renewable feed stocks, primarily biomass, is crucial to green chemistry. The entire biomass utilization process is guided by the green chemistry principles. It is not possible to view using biomass for chemistry as a goal in itself if all other green chemistry criteria are upheld. When biomass is employed, all of the above criteria also apply: efficiency of reactions, atom economy, restriction of resource consumption, prevention of waste, and safety of processes and products. These criteria cover biomass generation, conversion to biobased products, and final utilization. It's true that a number of significant and varied obstacles continue to restrict the range of biobased compounds that have made it to market, despite receiving favourable reviews for both sustainability and economy [12].

- The design of particular catalysts with the right stability and activity in highly oxygenated media is necessary for reaction efficiency and selectivity. These catalysts must be able to address the multifunctional nature of biomolecular substrates and anticipate the stability of the target product to prevent the formation of undesirable overtransformed products [12].
- The creation of novel, atom-economic, clean transformations of biomolecules and platform molecules is necessary for the revitalization of biobased chemistry. This will increase the range of building blocks that are accessible and promote the identification of novel compounds with unique molecular designs [12].
- By dissolving strongly bonded and polar materials, appropriate media which have benefited from advances in the fields of ionic liquids, smart mixes with catalysts, and deep eutectic solvents offer substitutes for the organic solvents that were previously used [12].

B. **Surfactant in Green Corrosion Control-**

Surfactants are good corrosion inhibitors because they have certain necessary properties. Numerous writers investigated how well surfactants inhibited various metal/electrolyte systems. There are comparatively few studies on the anticorrosive properties of biosurfactants, or surfactants made from microbes and plants. This is a result of their costly and time-consuming purification, characterization, extraction, and identification processes [16].

C. **Natural Polymer-**

Natural polymers are derived from living things, such as plants and animals. The existence of these polymers is required for life. Example- Starch, cellulose, proteins, nucleic acid etc [10].

- In the food, cosmetic, and pharmaceutical sectors, xanthan gum is frequently used as an emulsifier, thickener, and stabilizer.
- Guar gum is used as a thickening in sauces and cosmetics. It is employed to prevent ice crystals from forming in ice cream.

Additionally, it can be employed in the manufacturing of tablets with prolonged release.

- Acacia is used as a suspending agent, emulsifying agent and tablet binder.
- As a hydrophilic polymeric substance, pectin holds great promise for use in controlled release matrix drug delivery systems [10].

D. Silver Nanoparticles Synthesis-

Synthesis of silver nanoparticles, which are compounds made by flora, bacteria, or plants that function as stabilizing and reducing agents. The primary agents responsible for the biologic creation of nanoparticles are either plant phytochemicals with reducing or antioxidant qualities, or microbial enzymes [17].

E. In Day-to-day Activities-

- The solvent most frequently used in dry cleaning garments is percholoroethylene. When disposed of, it contaminates ground water and is thought to be carcinogenic. Joseph De Simons, Timothy Remark, and James Mcclain created a novel technique called miCell technology that allows liquid carbon dioxide to be utilised as a safer solvent in combination with a surfactant for dry cleaning clothing. Certain dry cleaners are currently using this technique on a commercial basis. Green solvent has been used in place of the carcinogen perchloroethylene in dry cleaning machines [1].
- Powdered tamarind seed kernels, which are typically thrown away as agricultural trash, work well as a clearing agent for industrial and municipal waste [1].
- Traditionally, the lignin from the wood used to make high-quality white paper is eliminated by immersing tiny wood fragments in a solution of sodium hydroxide and sodium sulphide, then watching as the wood reacts with chlorine. During the process, chlorine also combines with the lignin's aromatic rings to create chlorinated furans and dioxins. These substances cause health issues because they are carcinogens. In order to create a green bleaching agent, Terrence Collins of Carnegie Mellon University used H_2O_2 as a bleaching agent in the presence of activators like TAML, which catalyzed the quick conversion of H_2O_2 into hydroxyl radicals, which induce bleaching. Lignin is broken down by this bleaching chemical at a considerably lower temperature and in a shorter amount of time. It reduces the amount of water needed for laundry [1].
- The pharmaceutical business is trying to create drugs with fewer negative side effects using techniques that result in less lethal waste. A second-generation green synthesis of sitagliptin, an active component of the type 2 diabetes medication Januvia, was created by Merck and Codexis. This produced an enzymatic method that increases yield, improves safety, decreases waste, and does away with the need for a metal catalyst [1].

F. Water-based green photocatalytic synthesis-

It has been established that water, an easily accessible and non-toxic natural resource, is an excellent green medium for organic processes. Water's use as an environmentally friendly reaction medium for organic reactions has drawn a lot of interest. For instance, in the late 2000s, Chao-Jun Li's lab created a number of catalytic nucleophilic additions of terminal alkynes in water. Since then, it has become common practice in contemporary organic chemistry to substitute water for traditional organic solvents. Water has proven to be an effective green medium for both homogeneous and heterogeneous photocatalytic organic processes over the last ten years [18].

CONCLUSION:

The main purpose of this paper to provide information about green chemistry and its application in the Pharmaceutical industries, it is clear that, with the application and expansion of its tenets, Green Chemistry is a novel conceptual approach that has the potential to support sustainable development. Even though the use of Green chemistry has increased over the last few years, very few chemical firms worldwide have strategically used it. Though much work remains, the pharmaceutical sector has risen to the challenge and is making significant strides towards substituting more environmentally friendly, sustainable alternatives for outdated procedures. A significant foundation for overcoming these undesirable, hazardous compounds is offered by green chemistry. It creates a broad and varied research avenue for the development of more effective reaction processes that reduce waste and increase the targeted product yield. Green chemistry is expanding rapidly and offers a proactive path for the sustainable advancement of science and technology in the future. This path can be helpful in designing highly effective, eco-friendly synthetic practices and procedures that can produce life-saving medications and expedite lead optimization in drug discovery while minimizing environmental degradation.

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