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The application and prospect of green chemistry in pharmaceutical field

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Abstract. As the global environmental problem gets worse and worse, green chemistry as a sustainable theory and method gets more attention than before. This paper talks about green chemistry in the pharmaceutical industry. Initiate the discussion by introducing green chemistry and its twelve principles, highlighting the methods and technologies of green synthesis. Next, the research will discuss the environmental challenges that the pharmaceutical industry faces, the detrimental effects of traditional processes on the environment, and the analysis required to transition to a greener approach. Next, it delves into the two aspects of green chemistry's application in the pharmaceutical field: green synthetic drugs, green solvents, and green catalysts. Next, it presents a summary of the advancements and future potential of green chemistry technology. Finally, the paper found that using the principle of atom economy properly can minimise the generation of by-products and reduce the after-treatment cost. What's more, the solvent, which always took up a large amount of total mass, used a lot of resources but resulted in a lower conversion rate.

Keywords: green chemistry, green synthesis, pharmaceutical field, catalysis

1. Introduction

Green chemistry, a new branch of chemistry [1], is a term for designing chemical processes by controlling the use and production of toxic substances. The pharmaceutical field is positively evolving in the production of medicines, thereby enhancing people's well-being and becoming increasingly significant in our daily lives. Medicine protects us from injury and disease, thereby reducing death. However, as the manufacturing of chemicals progresses quickly, incorrect purification or treatment leads to the production of undesirable intermediates and products, causing further deterioration. This leads to an increase in the level of pollutants in the environment, which then causes deterioration. Furthermore, as the severity of the global problem escalates, Pollutant emissions and significant resource consumption during traditional processes are increasingly attracting people's attention. As a result, people are turning to green chemistry as a sustainable development method that can partially solve problems and provide an orientation for the pharmaceutical field. How do you apply green chemistry to the pharmaceutical field? Scientists continue their research, applying nearly all the principles of green chemistry to it. The purpose of this paper is to deeply analyse the application of the twelve principles of green chemistry in the pharmaceutical field and its mitigation of environmental challenges in order to make the pharmaceutical industry more sustainable.

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2. Definition and principles of Green Chemistry

Green Chemistry focuses on the molecular level, making chemical reactions, processes, and products more environmentally friendly and reducing the hazardous and toxic chemical substances that are used and generated. It is also defined as “sustainable chemistry,”, a branch of chemistry that eliminates waste emergencies that are harmful to human health or the environment, designs better “atomic economy” of chemical reactions, and achieves “zero discharge” of waste [1].

As humans enter the 21st century, more stringent environmental protection regulations and the high cost of dealing with pollutants have prompted the chemical industry to focus on eliminating or reducing the production of waste from the source, rather than polluting and then treating, so green synthesis has emerged.

The concept of green synthesis comes from green chemistry; it refers to the fact to the fact that in the process of chemical synthesis, try to use environmentally friendly, low-toxic, and efficient methods to synthesise organic compounds. Green organic chemical synthesis technology emphasises the selection of renewable resources or low-toxicity and harmless materials. These renewable resources can come from plants or microorganisms, such as extracts of natural plants and biomass.

Biomass includes several components: cellulose, proteins, sugars, and so on. Each of them can be transformed into various chemicals, from simple alcohols to polymers and specific chemicals. It is easily found in our lives, especially in rural areas, and this can increase farmers’ extra income. By using biomass, we can avoid sanctions from other countries that are full of petroleum [2].

With these renewable resources, humans can not only reduce their dependence on fossil energy but also minimise environmental pollution. In addition, low-toxicity and harmless materials can also avoid the harm of residual harmful substances to the environment and health.

The following will introduce the twelve principles of green chemistry.

2.1. Prevention & Atom Economy

Designing chemical reactions and processes to prevent the creation of waste. Consider the generation of waste at first instead of clearing up the waste after production.

Accurate waste quantification is essential to the Green Chemistry approach, offering precise standards that can be analysed for improvement and optimisation of chemical reactions and processes. There are two different ways to quantify waste: E-factor and Process Mass Intensity [2].

The environmental factor is the following used to measure the waste:

Environmental factor (E-factor) = kg waste/kg product

Based on the definition of E-factor, the pharmaceutical industry elaborated on a more comprehensive metric: process mass intensity (PMI) [2].

PMI=total weight of input (kg)/total weight of product (kg)

Designing the input to react as much as possible. Try to turn all reactants into final products, to increase the production of desired product, while reducing the waste.

Atom Economy=molar mass of desired products/molar mass of total reactants*100%

2.2. Less hazardous chemical syntheses & design of safer chemicals

Though some products do not contain toxic substances, there is still a risk of contamination; hence, we use green chemistry to redesign the processes. This principle is for designing the chemical reaction to generate substances with little toxicity; the main purpose is to avoid using hazardous chemicals at the beginning.

In chemical synthesis and production, we should design the chemicals to reach their desired function while minimising toxicity. What’s more, we have to maintain the balance between its function and safety. For instance, in pharmaceuticals, the safety of the drug compound is related to its ability to inhibit a particular enzyme [2]. Safety refers to the minimization of adverse effects when the chemical is used in the intended way, which also means less potential for toxicity and less environmental damage. Safety

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assessments typically include acute and chronic assessments; they cover impacts on human health, the environment, and potential exposures [2].

2.3. Safer solvents and auxiliaries & Design for energy efficiency

During the reaction, the use of solvents is necessary and cannot be avoided, so we should try to choose the solvents and auxiliary substances that are less harmful to humans and the environment. Generally, the solvent constitutes between 50 and 80% of the overall input mass; this percentage can vary depending on whether water is included in the calculation. Therefore, water dramatically affects the PMI [2].Due to their inherent properties, solvents often present potential hazards ranging from flammability to volatility; they all require rigorous precautionary measures.

Designing for energy efficiency aims to reduce energy consumption and utilize it effectively. Energy efficiency in chemical reactions is not just about reducing the total energy we use; it is also related to the type of energy we choose. Traditionally, the chemical industry severely depends on non-renewable resources for energy; however, in ideal conditions, the energy we use in chemical processes should always come from renewable sources, such as wind, solar, or hydropower. This can help to minimise the carbon footprint and ensure a sustainable approach to chemistry [2].

2.4. Use of renewable feedstocks & Reduction of derivatives

Chemical processes rely heavily on non-renewable resources, particularly fossil fuels, as primary feedstocks, putting heavy pressure on the development of sustainability. Therefore, choosing renewable raw materials can partially solve this problem. Biomass can be a good example; it has emerged as a remarkable renewable resource for chemical production that is abundant and a sustainable substitute for petroleum-based feedstocks [2]. It marks a shift in the industry's approach.

We should notice that although derivatives have contributed to simplifying the synthesis process, they have many adverse effects, such as extra energy consumption and the use of additional reagents. Therefore, we should try our best to avoid the unnecessary generation of derivatives, seek methods that can directly obtain the desired transformation without the need for these interim steps [2].

2.5. Use of catalysis & Design for degradation

Using catalysts can speed up the reaction. It helps most of the starting materials integrate into the desired product, significantly reducing waste. Its reaction specifically targets the product, leading to a reduction in by-products and waste. Reusing catalysts allows for a reduction in resource shortage due to their repeated use.

Designing for degradation involves treating chemical substances and breaking them down into harmless substances. However, degradation is not as easy as we think; their ability to degrade depends on carbon.

The backbone, stability under high heat, and resistance to hydrolytic and photolytic processes are crucial factors [2]. So, it is up to the degradation products' properties.

2.6. Real-time analysis for pollution prevention & Inherently safer Chemistry for accident prevention

Developing analytical methods to monitor a chemical process in real-time not only prevents the formation of hazardous substances polluting the environment and harming humans, but also, based on real-time data, makes chemical processes more efficient, with a higher yield and less waste production. Prevention is more important than treatment; it is its main aim [2].

Choosing substances and designing reaction conditions to minimise the potential accidents, such as explosions or fires. What's more, the chemical industry can result in costly downtime, legal liabilities, and reparative measures [2]. By designing inherently safer chemistry, industries can enhance operational efficiency and foster trust among their consumer base and the broader public.

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3. Environmental challenges of the pharmaceutical industry

With the impact of climate change becoming more and more serious, chemical drugs have been listed as one of the key polluting industries by the state, and have become the industry that the state focuses on in terms of energy conservation and emission reduction [3].

The traditional pharmaceutical process is often accompanied by a lot of waste generation, high energy consumption, organic solvent use, and other problems that have serious impacts on the environment. The most important one is the Three Wastes, which refer to the waste water, waste gas, and waste residue produced in the production process.

Because of the pollution from traditional synthesis methods, chemical bulk drugs always cause a large amount of pollution, and many kinds of pollutants have high toxicity. The production of bulk drugs requires a high consumption of energy and resources, so the production process and reaction steps are complicated. The number of raw materials inputs is large, and the conversion rate to the desired products is low. Therefore, there is a need for more environmentally friendly and greener synthesis methods.

At the beginning of the 21st century, the Chinese government realised that the industrial structure of the pharmaceutical industry was not reasonable, there were many low-quality products, and the pollution of chemical bulk drugs was difficult to control. The government successively introduced relevant policies and industrial emission standards to encourage enterprises to increase transformation and upgrading, implement cleaner production, and protect the environment. There are two technologies that have already been used, such as emission reduction measures on the source and terminal treatment technology [4].

4. Application of green chemistry in pharmaceutical field

4.1. Green synthetic drug and green solvents and catalysts

Applying the atomic economic principles of green chemistry in pharmaceutical research and development, which design the chemical reaction to make more desired products with less waste, can effectively reduce the generation of by-products and storage and disposal costs.

Solvent can significantly influence costs. Because in standard chemical operations, the solvent usually accounts for 50%–80% of the mass, resulting in a large consumption of energy.

What's more, catalysts are a crucial component of green organic chemical synthesis technology. Choosing efficient catalysts to improve the reaction rate and selectivity can reduce the temperature and pressure conditions during the synthesising process, thereby reducing energy consumption [5].

4.2. Case study

"For example, Merck has developed a greener way to produce molnupiravir, an antiviral drug used to treat COVID-19. Reduced the solvent waste, increasing production by 1.6 times, and shorten the five-step process to three steps. In 2022, the United States Environmental Protection Agency awarded it a Green Reaction Condition Award for this synthetic method."

"Amgen developed the green synthesis of LUMAKRAS™, a new drug for the treatment of certain non-small cell lung cancers. About the reduction in purification steps that produce large amounts of solvent waste, saving £3.17 million per year and increasing production. In 2022, the United States Environmental Protection Agency also awarded it a Green Reaction Condition Award for this synthetic method" [6].

5. Conclusion

Drug synthesisers develop green processes to avoid releasing harmful and toxic by-products into the environment. After analysing the application of the twelve principles of green chemistry in pharmaceuticals, this paper discovered that these principles are similar yet distinct; they both serve the same objective, namely designing experiments to decrease pollution and boost yield. However, each principle focuses on distinct aspects of the equation and occupies distinct positions in the reaction. Here

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are some examples of applications based on the twelve principles that this paper will enhance the transition towards a more environmentally friendly lifestyle:

Firstly, instead of petroleum-based feedstocks, use renewable resources as the primary feedstock. Renewable sources, such as wind, solar, or hydropower, can provide energy and improve energy efficiency.

Secondly, using biomass as a raw material can be partially beneficial. Biomass, derived from plant and organic waste, can help capture and store the carbon dioxide in the atmosphere. Since plants use biomass to produce chemicals, they can balance this carbon dioxide release by absorbing it during their growth. This feedstock can ensure a sustainable approach to chemistry.

Thirdly, reducing the use of water, which has a high content in the solvent, will dramatically impact the value of PMI. Because of the high water content, the solvent accounts for between 50 and 80% of the overall input mass, as this paper previously stated.

Finally, catalysts play a significant role in chemical reactions, improve the atom economy, and promote energy-efficient processes. Its tendency to react with specific products reduces the production of unwanted by-products and waste. Furthermore, the multiple uses of catalysts can result in significant resource savings.

When it comes to the new progress and prospect of green chemistry technology, the pharmaceutical industry will have a more sustainable and environmentally friendly future. From the improvement of fermentation efficiency, enzymatic conversion process, green crystallization technology, enhanced detoxification of antibiotic residues in wastewater, efficient and low-cost treatment of wastewater and other whole-process control research, these are the progress can support the sustainable development of the pharmaceutical industry [5].

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