



GREEN CHEMISTRY IN PHARMACEUTICAL RESEARCH

Deepa Chauhan*

Dept of Chemistry M.S.College Saharanpur (U.P.).

*Corresponding Author: Deepa Chauhan

Dept of Chemistry M.S.College Saharanpur (U.P.).

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Green chemistry expresses an area of research developing from scientific discoveries about pollution awareness and it utilizes a set of principles that reduces or eliminates the use or generation of hazardous substances in all steps of particular synthesis or process. Chemists and medicinal scientists can greatly reduce the risk to human health and the environment by following all the valuable principles of green chemistry. The most simple and direct way to apply green chemistry in pharmaceuticals is to utilize eco-friendly, non-hazardous, reproducible and efficient solvents and catalysts in synthesis of drug molecules, drug intermediates and in researches involving synthetic chemistry. Microwave synthesis is also an important tool of green chemistry by being energy efficient. Green chemistry expresses an area of research developing from scientific discoveries about pollution awareness and utilizes a set of principles that reduces or eliminate the use or generation of hazardous substances in all steps of particular synthesis or processes. Green chemistry, a sustainable chemistry, refers to environmental friendly chemicals and processes that result in: reduced waste, eliminating costly end-of-the-pipe treatments; safer products; and reduced use of energy and resources-all improving the competitiveness of chemical manufactures and their customers.

Green chemistry is the process of the "utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products."

Some principles are to be followed to attain the success for Green chemistry.

1. Prevention: It is better to prevent waste than to eat or clean up waste after it has been created.

2. Atom economy: Synthetic methods should be designed to maximize the incorporation of all materials used in the process of final product.

3. Less hazardous chemical syntheses: Wherever practicable, synthetic methods should be designed to use and generate substances that possess little or no toxicity to human health and the environment.

4. Designing safer chemicals: Chemical products should be designed to affect their desired function while minimizing their toxicity.

5. Safer solvents and auxiliaries: The use of auxiliary substances (e.g. solvents, separation agents, etc) should be made unnecessary wherever possible and innocuous when needed.

6. Design for energy efficiency: Energy requirements of chemical processes should be recognized for their environmental and economic impacts and should be minimized. If possible, synthetic methods should be conducted at ambient temperature and pressure.

7. Use of renewable feedstock: A raw material or a feedstock should be renewable rather than depleting whenever technically and economically practicable.

8. Reduce derivatives: Unnecessary derivatization (use of blocking groups, protection/deprotection, and temporary modification of physical/chemical processes) should be minimized or avoided if possible, because such steps require additional reagents and can generate waste.

9. Catalysis: Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.

10. Design for degradation: Chemical products should be designed so that at the end of their function they break down into innocuous degradation products and do not persist in the environment.

11. Real-time analysis for pollution prevention: Analytical methodologies need to be further developed to allow for real time, in process monitoring and control prior to the formation of hazardous substances.

12. Inherently safer chemistry for accident prevention: Substances and a form of substance used in a chemical process should be minimized to choose to minimize the potential for chemical accidents, including releases, explosions and fire.

Green chemistry incorporates concepts such as atom economy, convergence- higher process efficiency with fewer operations, reagent optimization by use of catalysis and more selective and recyclable reagents, and raw material efficiency. Green chemistry and

engineering for achieving substantial decreases in solvent and raw materials use and waste by replacing chemical transformation steps with bio catalytic alternatives. The strategy in biochemical transformations is to modify the entire synthetic route by generating new intermediates and reducing the number of reaction steps, while minimizing energy input and waste. The outcome is to use of enzymes as biocatalysts in large number of chemical processes to increase product yield. Another trend in green chemistry is the move away from extraction of pharmaceuticals and toward isolation of the product directly from the process stream, by crystallization followed by filtration. Compared to preparative chromatography, direct isolation might have a lower yield, but it offers the advantages of decreased cycle times and labor costs, less waste, and fewer steps so there are fewer opportunities for contamination or product loss.

Green Chemistry in Pharmaceuticals

Environment management is vital to pharma companies as the final products have to be of the highest purity. Therefore pharma sector have to follow stringent quality control norms. This is even more necessary as the pharma industry is considered a waste-intensive industry; the ratio of waste to product is often 10:1. The initiatives taken to improve the environmental impact of a given process, mostly has a positive impact. The Market leaders review continuously their manufacturing processes to make them environmentally as harmless as possible and cost-effective.

Some of the worst examples of atom inefficiency and relative quantities of waste are to be found in the industry. The E factor (total waste/product by weight) is a simple but quite comprehensive measure of process efficiency and commonly shows values of 100+ in drug manufacture. This can be largely attributed to the complex, multistep nature of these processes. Typically, each step in the process is carried out separately with workup, isolation, and purification all adding to the inputs and amount of waste produced.

The Indian pharma industry is following norms as far as environmental management is concerned. However, there are innumerable smaller drug manufacturing units which flout the rules and releasing higher-than permissible levels of antibiotics enter the local water bodies, which could destroy the ecological balance. The initiatives taken to improve the environmental impact of a given process, has a positive impact, most of the time, on the cost economics of that process.

Advances in enzymatic catalysis of synthetic reactions, solvent substitutions, and recycling of by products and waste may not only reduce the environmental impact of pharmaceutical processes, but with the potential to have a positive effect on synthetic efficiency and overall productivity, can also decrease waste streams, lessen energy input, and minimize the need for hazardous reagents. These developments can put green in the form

of lowering the manufacturing costs. The pharma sector has to demonstrate the potential for applying waste-prevention strategies to improve the cost-effectiveness of manufacturing.

Not only are green principles and practices becoming more main stream in process chemistry, but they are also at the forefront of a movement to make environmental impact a priority upfront in the design of R&D and manufacturing processes. The emphasis in industry has been on designing the most efficient and rapid synthesis route. As the environmental impact and costs associated with disposing of toxic solvents and waste products have come to the forefront, greater emphasis is being given to reducing waste streams and minimizing energy input. The environment and economy are twin partners in the pursuit of quality existence. The initiatives taken to improve the environmental impact of a given process, has a positive impact, most of the time, on the cost economics of that process. In view of this, industry should continuously review their manufacturing processes to make them environmentally as harmless as possible and cost-effective.

Pharmaceutical companies can influence and improve the environmental performance with utilizing green chemistry. Green chemistry is being employed to develop revolutionary drug delivery methods that are more effective and less toxic and could benefit millions of patients, some of them are described here. Phosphoramidite-based, solid-phase synthesis of antisense oligonucleotides has been modified to accommodate principles of green chemistry by eliminating the use and generation of toxic materials and allowing reuse of valuable materials such as amidites, solid-support and protecting groups, thus improving the atom economy and cost-efficiency. Pharmaceuticals can enter the environment in several ways.

1. Excretion after therapeutic use.
 2. Discharge of treated wastewater from manufacturing facilities.
 3. Disposal of unused medicine by patient-consumers.
- So there is a significant role of pharmaceutical companies to help in this GO-GREEN program, some companies have already started with the process like
1. Using more environment friendly product to replace organic volatile material in manufacturing process.
 2. Repairs production line to reduce CO₂ emissions and energy consumption.
 3. Lowers the amount of purified H₂O used in productions of pharmaceuticals.
 4. Reduces landfill waste through provision of reusable clothing for employees (v. disposable).
 5. Optimizing HVAC, using high efficiency lightning.
 6. Zeroing in their manufacturing processes, not only to get drugs to market sooner but to reduce the overall environmental impact of development and commercial manufacture. Companies including GSK and Pfizer have developed tables which list undesirable solvents and suggest suitable

replacements, and such programmers have cut by almost two-thirds the amount of dichloromethane used at Pfizer's three main research sites, while the use of di isopropyl ether has been eliminated entirely. These tablets are also used for common chemical transformations, such as the oxidation of alcohols to aldehydes.

7. The companies like Pfizer who's chemists also went green for the synthesis of pregabalin for which they won the astra veneca green chemistry award also.
8. The industry is also starting to analyse the green credentials of chemical feedstock bought in from external suppliers.
9. The solvents are evaluated using nine factors in several areas, which include worker safety, process-safety, environmental, and regulatory assessments.

For implementation of green chemistry all these principles must be well considered and practiced. I have focused on solvents and catalysts which can be used as Green Solvents and Green catalysts, which comprise an important part of almost all type of organic reactions.

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