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A Review on Green Chemistry in Pharmacy

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1. ABSTRACT: -

Green chemistry Manufacturing and improving chemical processes that reduce or avoid the use of harmful substances. In the pharmaceutical field, it plays an important role in making drug manufacturing more sustainable by solving problems like high solvent consumption, formation of toxic waste, and energy-heavy production steps. This review explains the twelve principles of green chemistry and shows how they are used in pharmacy through safer solvents, catalytic reactions, better atom utilization, and continuous-flow methods. It also highlights the importance of green analytical chemistry in promoting environmentally safe testing and quality control. Recent developments such as biocatalysis, deep eutectic solvents, renewable raw materials, and AI-based process optimization are also discussed. While there has been good progress, industries still face challenges such as cost, large-scale application, and regulatory issues. Overall, green chemistry provides a sustainable and responsible approach for producing safer, more economical, and eco-friendly pharmaceutical products.

Keywords: -Green chemistry, sustainable pharmacy, green analytical chemistry, pharmaceutical industry, eco-friendly synthesis, catalysis, renewable solvents.

2. INTRODUCTION: -

Green Chemistry, also called sustainable chemistry, is an area of chemistry and chemical engineering focused on the design of products and processes that minimize or eliminate the use and generation of hazardous. Green Chemistry is a science-based philosophy of designing chemicals, products, and processes with the intention of making them less hazardous and more sustainable.[1]

Fig.1: - Glowing Green Chemistry Experiment.

Ref: - Experiment

3. HISTORY AND ORIGIN OF GREEN CHEMISTRY: -

In the 1960s, the publication of the book 'Silent Spring' opened the eyes of many. The scientific book raised awareness about ecological perception and has shown the risks associated with the over-use of natural resources. The book described how certain chemicals are affecting our ecosystem. The EPA or Environmental Protection Agency was launched in 1970. The Stockholm conference was conducted in 1972 in Sweden, which was attended by many countries along with the members of the United Nations In this conference, the members discussed the environmental damages that cause the depletion of the ecosystem and alert everyone regarding the same. Till the 1980s, the chemical industry and the EPA concentrated mainly on pollution and harmful toxins. However, a significant shift occurred among chemists as scientists started spreading environmental awareness and researching avenues to prevent pollution. The Organization for Economic Co-operation and Development (OECD), an international body.[2]

In the year 1990 Pollution Prevention Act was passed in US. The act gives a path to the growth of new and inventive approach to handle with pollution and hazardous substances. The green chemistry idea was made possible as a result. The two-letter phrase "Green Chemistry and its twelve principles were created by Paul Anastas and John Warner.[3]

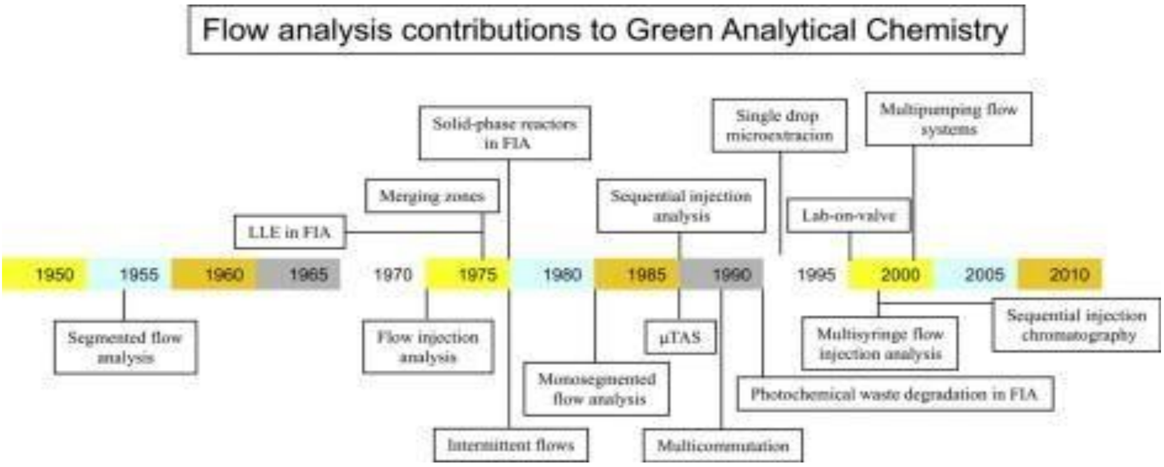

Fig 2: - Flow analysis contributions to Green Analytical Chemistry.

Ref: - Analysis

4. PRINCIPLES: -[4]

Green chemistry in pharmaceuticals is guided by principles such as atom economy, less hazardous chemical syntheses, safer solvents, energy efficiency, and the use of renewable feedstocks.

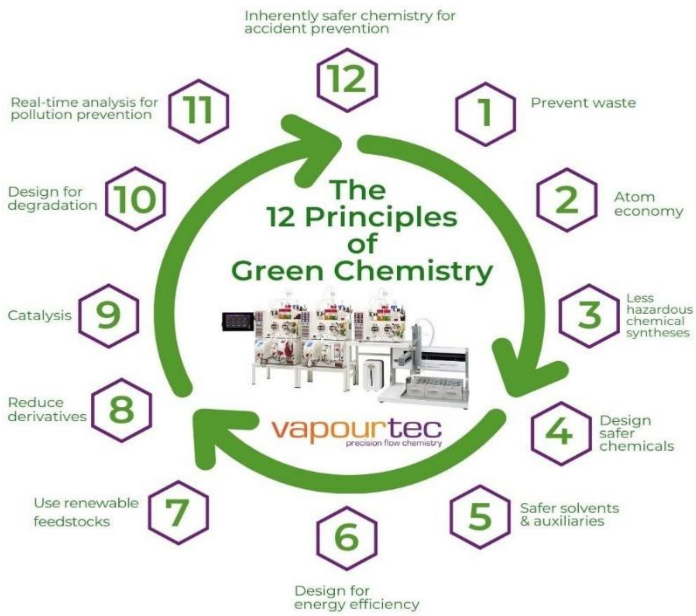

Fig 3: - The 12 Principles of Green Chemistry.

Ref: - Principles

- **Prevention of Waste**

The first principle focuses on waste prevention, encouraging processes that avoid generating waste instead of treating or disposing of it later. In the pharmaceutical industry, this approach reduces the overall environmental impact of drug production by designing reactions with minimal byproducts. As Sheldon points out, waste minimization aligns with sustainability goals, particularly when aiming to reduce the high Environmental Factor in pharmaceutical manufacturing.

- **Atom Economy**

Atom economy refers to designing synthetic methods where the maximum proportion of reactants are incorporated into the final product. High atom economy processes minimize waste, reduce costs, and increase resource efficiency, as noted in pharmaceutical synthesis reactions that use efficient catalysts or streamlined routes to achieve maximum yield.

- **Less Hazardous Chemical Synthesis**

This principle encourages using and generating substances with little to no toxicity, aiming to reduce harmful impacts on both human health and the environment. For instance, the development of non-toxic catalysts for pharmaceutical reactions has enabled safer chemical synthesis pathways.

- **Designing Safer Chemicals**

Safer chemical design involves creating molecules with the desired efficacy but reduced toxicity. In the pharmaceutical industry, this principle underpins drug design processes that focus on minimizing adverse effects, thus improving the safety profile of synthesized compounds.

- **Safer Solvents and Auxiliaries**

Traditional solvents, often toxic and non-biodegradable, contribute substantially to the pharmaceutical industry's environmental footprint. Green chemistry promotes the use of alternative solvents, such as water, bio-based solvents, and supercritical Co2. which are safer for the environment and reduce volatile organic compound (VOC) emissions.

- **Design for Energy Efficiency**

Energy-intensive processes not only elevate costs but also increase the environmental burden due to high emissions. This principle emphasizes designing energy-efficient reactions, such as using microwave-assisted synthesis or flow chemistry, which reduce energy requirements and reaction times.

- **Use of Renewable Feedstocks**

The seventh principle focuses on using renewable resources rather than depleting non- renewable feedstocks. In pharmaceutical synthesis, this has led to the exploration of bio-based materials as starting compounds, thereby supporting sustainable resource utilization.

- **Reduction of Derivatives**

Unnecessary derivatization steps often involve using additional chemicals and generating waste. Avoiding such steps aligns with green chemistry by simplifying synthesis routes and minimizing waste, which is essential for efficient pharmaceutical manufacturing.

- **Catalysis**

Catalysis is a cornerstone of green chemistry, enabling efficient chemical transformations that minimize energy consumption and waste. Catalytic reactions, particularly biocatalysis and metal-catalysed processes, have been instrumental in pharmaceutical synthesis, increasing reaction selectivity and reducing harmful byproducts.

❖ Design for Degradation

This principle focuses on designing molecules that break down into non-toxic byproducts after their intended use, thereby reducing environmental persistence. Pharmaceuticals that degrade into harmless compounds minimize ecological impact, addressing concerns related to bioaccumulation and persistence in water sources.

❖ Real-time Analysis for Pollution Prevention

The use of real-time analytical techniques helps to monitor and control chemical processes, ensuring minimal waste generation and enhanced efficiency. Process analytical technology (PAT), for example, has become essential in pharmaceutical manufacturing. allowing for in-process adjustments that improve yields and reduce waste.

❖ Inherently Safer Chemistry for Accident Prevention

The final principle emphasizes designing chemical processes that minimize risks associated with explosions, fires, and accidental releases. In pharmaceutical synthesis, this involves using non-volatile and less reactive chemicals, reducing the potential for hazardous incidents.

5. METHODS: -

These are some methods in green chemistry in pharmacy.

Green Chemistry in Pharmacy

Method	Example	Benefit
Solvent Selection	Use green solvents, such as water, ethanol, supercritic CO_2, and Ionic liquids	Reduce toxic organic solvents
Use of Biocatalysts	Enzymes or microbial systems replace harsh chemical catalysts	Mild reaction conditions, high selectivity less waste
Solvent-free or Microwave-assisted synthesis	Microwave-assisted synthesis of paracetamol faster and more	Reduced reaction time, and solvent use
Green Formulation Techniques	Nanoformulations and liposomes prepared by ethanol injection or super-critical fluid method	Eco-friendly formulations
Use of Renewable Raw Materials	APIs or excipients from plant-based or biodegra dable sources	Renewable raw materials
Atom Economy & Waste Minimization	Designing reactions that use all atoms from reactants in the final product	Fewer steps less waste
Energy Efficiency	Conduct reactions at ambient temperature and pressure	Energy efficiency
Green Packaging	Blister packs from bioplastics or recycled paperboard	Reduction packaging waste

Fig 4: - Methods of Green Chemistry in Pharmacy Ref: - Methods

1. **Solvent Selection:**

Choosing environmentally friendly solvents or water-based formulations for agrochemicals. This minimizes the use of toxic solvents, reducing harm to ecosystems and promoting the safety of agricultural workers.[5]

2. **Green Analytical Techniques:**

Utilization of environmentally friendly analytical methods to monitor and control pharmaceutical processes. Implementation of techniques such as green chromatography and spectroscopy.[5]

3. **Eco-friendly Packaging:**

Consideration of green chemistry principles in the design and production of pharmaceutical packaging. Exploration of sustainable and biodegradable packaging materials. Life Cycle Assessment.[5]

4. **Catalysis and Biocatalysis:**

Catalysis plays a crucial role in green chemistry by enabling more efficient and selective reactions while minimizing the use of stoichiometric reagents and energy inputs. Traditional catalytic processes often involve transition metal catalysts, which can be expensive, toxic, and non-renewable.!"" Green catalysis focuses on the development of catalysts that are environmentally benign, renewable, and highly efficient. Biocatalysis, a subset of green catalysis, utilizes enzymes and other biological catalysts to perform chemical transformations with high selectivity and specificity under mild reaction conditions. Biocatalysts are derived from renewable resources, such as microorganisms, plants, and enzymes engineered through protein engineering techniques. Biocatalytic reactions-typically occur-in aqueous environments at ambient temperatures and pressures, reducing energy consumption and minimizing waste generation.[6]

5. **Microwave and Ultrasonic-Assisted Synthesis:**

Microwave and ultrasonic-assisted synthesis Are innovative techniques that offer several advantages over traditional heating methods in pharmaceutical synthesis. These methods utilize electromagnetic radiation (microwave) or mechanical vibrations (ultrasonic) to enhance reaction rates, improve yields, and reduce reaction times! By applying energy directly to the reaction mixture, microwave and ultrasonic-assisted synthesis can accelerate chemical reactions and promote higher levels of selectivity and efficiency. Microwave-assisted synthesis involves heating reaction mixtures using microwave radiation, which selectively heats polar molecules and generates localized heating effects!" I This results in faster reaction kinetics, reduced energy consumption, and improved yields compared to conventional heating methods. Ultrasonic-assisted synthesis utilizes high-frequency sound waves to create cavitation bubbles in the reaction mixture, promoting mixing and enhancing mass transfer rates. This leads to shorter reaction times, increased yields, and improved product purity.[6]

6. **Atom Economy and Minimizing By-products:**

A basic idea in green chemistry is the atomic economy, which measures how many atoms of the original ingredients enter the final product to determine the efficiency of the chemical process. Because most of the original ingredients are used in the final product, high atomic efficiency indicates a low waste production. Pharmacological synthesis processes can reduce the total waste production and the formation of by- products by optimizing the atomic economy.[6]

7. **Use of Renewable Energy:**

Renewable energy obtained from biomass such as sugars, oils, and plant-based molecules is being increasingly pursued by the pharmaceutical industry as starting materials for drug synthesis. These green resources not only ensure the reduction of reliance with respect to petroleum-based raw materials but also develop a circular economy by recycling waste products made from the production of the ago and food industries. Production of drugs from bio-based feedstocks can reduce the carbon footprint of pharmaceutical manufacturing and contribute to alleviation of the fears on depleting resources.[7]

6. INDUSTRY PRACTICES: -

1. Use of Greener Solvents.

Green chemistry encourages using safer solvents like water, ethanol, or supercritical CO_2 instead of toxic organic solvents. These greener alternatives reduce environmental harm, lower waste, and make pharmaceutical processes safer and more sustainable.[8]

2. Catalysis for Cleaner Reactions.

Catalysts help reactions happen faster, with less energy and fewer chemicals. Using biocatalysts or eco-friendly catalysts improves reaction selectivity and reduces harmful by-products, making pharmaceutical synthesis cleaner and more efficient.[9]

3. Continuous-Flow Manufacturing.

Continuous-flow systems allow reactions to run steadily instead of in batches. This improves safety, reduces solvent use, saves energy, and gives better-quality products. It is now widely adopted for greener drug manufacturing.[10]

4. Waste Reduction and Resource Efficiency.

Green chemistry promotes using materials wisely through atom economy, solvent recycling, and cleaner reaction pathways. These approaches help reduce hazardous waste and make pharmaceutical production more economical and eco-friendlier.[11]

5. Renewable and Bio-Based Raw Materials.

Using raw materials from plants, sugars, or oils instead of petroleum-based chemicals reduces pollution and dependence on non-renewable resources. These bio-based materials support a sustainable and circular chemical industry.[12]

6. Energy-Efficient Technologies.

Techniques like microwave heating, ultrasounds, and low-temperature reactions help save energy in pharmaceutical processes. These technologies make reactions faster and reduce the overall environmental impact of drug synthesis.[13]

7. Green Analytical Techniques.

Eco-friendly analytical methods use less solvent, smaller samples, and faster techniques such as NIR or Raman spectroscopy. These methods reduce laboratory waste, save time, and support sustainable quality control.[14]

8. Digital & AI-Based Optimization.

AI and digital tools help predict reaction outcomes, optimize processes, and reduce the need for repeated experiments. This saves chemicals, energy, and time, making pharmaceutical development more efficient and greener.[15]

9. Pollution Control and Circular Manufacturing.

Green chemistry promotes recycling by-products, treating wastewater, and designing processes that reuse resources. This prevents pollution and supports circular manufacturing in the pharmaceutical industry.[16]

10. Industry Certifications & Global Standards.

Pharma companies follow standards like ISO 14001 and green manufacturing guidelines to prove their sustainability practices. These certifications encourage safer, cleaner, and more responsible production methods.[17]

7. GREEN CHEMISTRY AND PHARMACEUTICAL WASTEWATER MANAGEMENT: -

Green chemistry, defined as the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances, has gained significant attention in recent years as a sustainable solution to environmental pollution (Anastas & Warner, 1998). In the context of pharmaceutical wastewater management, green chemistry principles aim to develop treatment technologies that are environmentally friendly, energy-efficient, and capable of breaking down pharmaceutical pollutants without producing harmful by products.[18]

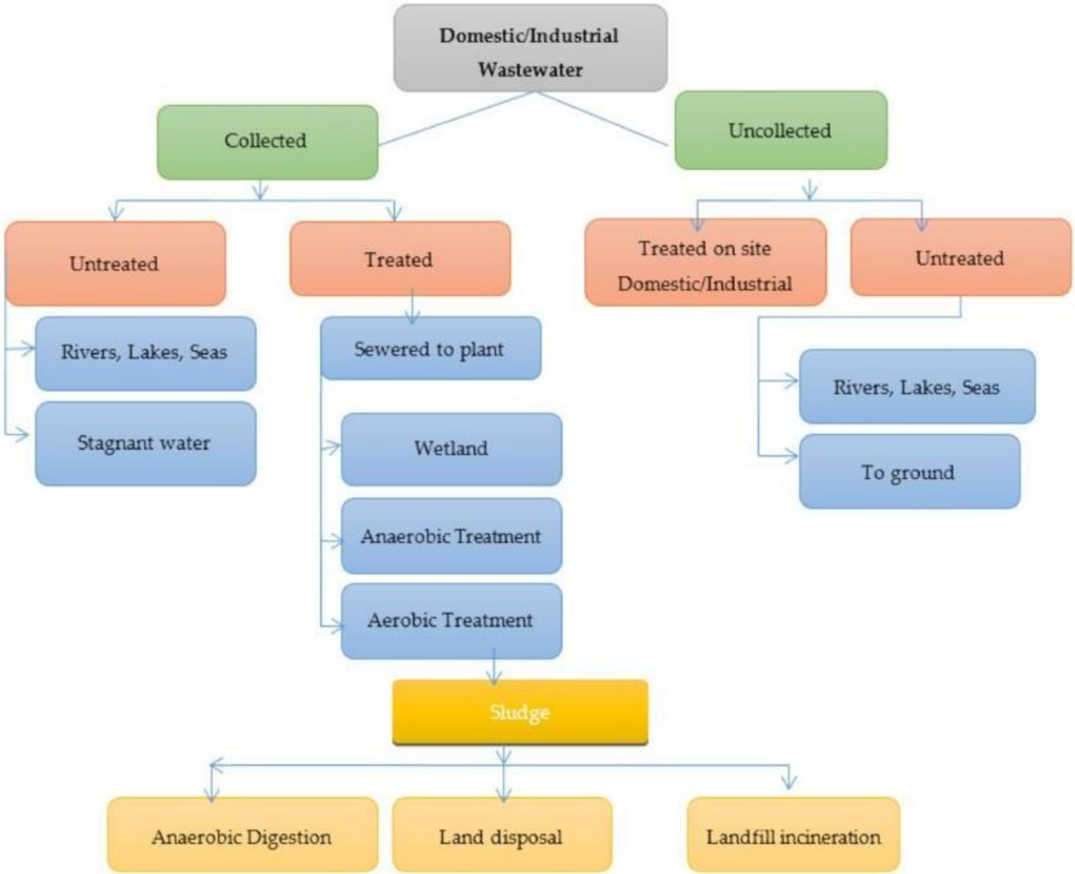

Fig 5: - Pharmaceutical Wastewater Management in Green Chemistry in Pharmacy Ref: - Waste management

8. REGULATORY ASPECTS OF GREEN CHEMISTRY: -

1. Environmental Protection Framework

Green chemistry follows the basic environmental laws that focus on preventing pollution and reducing harmful chemicals. Regulations guide industries to use safer chemicals, reduce emissions, and follow sustainable manufacturing practices. These rules ensure that pharma industries protect air, water, and soil quality.[19]

2. Indian Environmental Regulations

In India, green chemistry practices are connected to laws like:

- Environment Protection Act, 1986
- Air and Water Pollution Control Acts

These laws encourage industries to adopt eco-friendly processes, limit toxic releases, and use cleaner technologies during drug manufacturing.[20]

3. Hazardous Waste Management Rules

The Hazardous and Other Wastes Rules guide pharmaceutical companies on how to store, treat, transport, and dispose of chemical waste safely. These rules promote waste minimization, recycling, and proper disposal to avoid environmental damage. [21]

4. Regulations on Solvent Selection

Regulators encourage using safer solvents instead of toxic ones like benzene or chloroform. Guidelines from ICH and national regulators suggest using green solvents (ethanol, water) Solvent recycling methods This helps reduce pollution and improves worker safety.[22]

5. GMP and Pharmaceutical Manufacturing Standards

Good Manufacturing Practices (GMP) promote clean, safe, and controlled manufacturing. Under GMP and WHO guidelines, industries must use efficient processes, minimize waste, and ensure safe handling of chemicals throughout drug production.[23]

6. International Regulatory Influence

Global agencies like USFDA, WHO, and ICH encourage green chemistry by promoting safer raw materials, cleaner synthesis routes, and environmentally responsible manufacturing. Their guidelines support sustainable innovation in pharma industries worldwide.[24]

7. European Regulations

The EU REACH Regulation controls the use of chemicals and ensures they are safe for humans and the environment. It pushes industries toward non-toxic chemicals, renewable feedstocks, and energy-efficient manufacturing technologies.[25]

8. Regulations Promoting Cleaner Technologies

Many government programs promote technologies such as: Continuous-flow reactors Microwave/ultrasonic systems Solvent-recovery units These cleaner technologies help reduce emissions, energy use, and hazardous waste.[26]

9. Zero Liquid Discharge (ZLD) Compliance

In India, many pharma clusters must follow ZLD rules, which require companies to treat wastewater completely so that no liquid waste is released outside the facility. This supports water conservation and prevents water pollution.[27]

10. Regulatory Challenges

Industries face challenges like high cost of green technologies, lack of awareness, strict documentation requirements, and the need for skilled staff. Many companies struggle to switch from traditional methods to greener alternatives.[28]

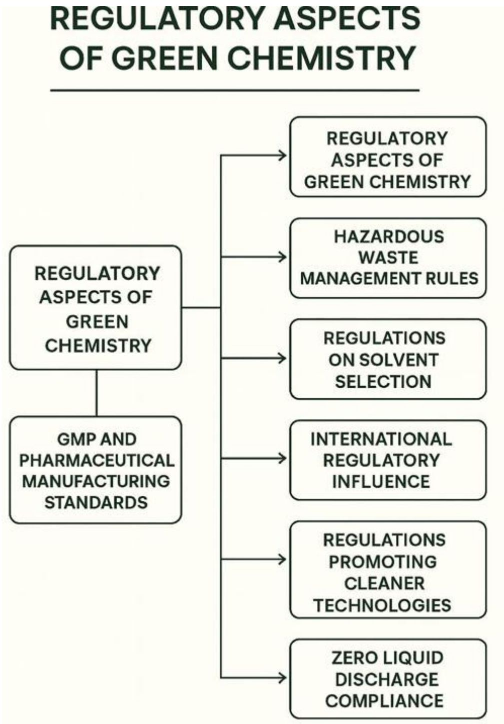

Fig 6: - Regulatory Aspects of Green Chemistry created by AI Ref: - Regulatory Aspects

9. ADVANTAGES AND DISADVANTAGES: - [29]

➢ **Advantages: -**

1. Reduced Environmental Pollution

Lower emissions, toxic waste, and resource consumption result in less harm to ecosystems and air/water quality.

2. Enhanced Safety

Using safer chemicals and solvents decreases the risk of occupational hazards and accidents in pharmaceutical labs.

3. Improved Cost-efficiency

Efficient reactions reduce resource use, energy costs, and waste disposal expenses, benefiting manufacturers economically.

4. Regulatory Compliance

Green chemistry supports compliance with stringent environmental and health regulations worldwide.

5. Sustainable Innovation

Encourages development of new eco-friendly technologies and practices that improve long-term viability of pharma industry.

6. Better Public Image

Green practices enhance a company's reputation and attract environmentally conscious investors and customers.

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- **Disadvantages / Limitations: -**

1. High Initial Costs

Transitioning to green technologies may require expensive equipment, R&D, and staff training.

2. Limited Availability of Green Reagents

Eco-friendly alternatives to some toxic reagents are still not widely available or commercially viable.

3. Scalability Challenges

Some green methods work in labs but are difficult to scale up for industrial production.

4. Technological Limitations

Not all pharmaceutical processes have green alternatives, which limits universal implementation.

5. Resistance To Change

Established companies may hesitate to adopt new methods due to inertia, uncertainty, or lack of awareness.

10. FUTURE TREND OF GREEN CHEMISTRY: - [30]

Future developments in green chemistry mainly focus on replacing harmful oxidizing agents and catalysts that often contain toxic heavy metals. These substances can damage human health and the environment, so scientists are working on safer alternatives. New ideas such as non- covalent chemistry and supramolecular chemistry aim to create reactions that can happen in the solid state without using solvents. Researchers are also exploring bio-based multifunctional reagents that can perform several roles in a reaction, making the process cleaner and more efficient. Combinatorial green chemistry is another growing area, where many different chemical compounds are produced quickly on a small scale using automated reaction systems. The expansion of solvent-free reactions also helps improve product separation and purification while reducing waste. These approaches make chemical processes safer, faster, and more sustainable.

Key Areas of Green Chemistry

- **Green Nano chemistry:**

Designing nanoparticles and nanomaterials using safe, eco-friendly methods.

- **Supramolecular Chemistry:**

Building chemical systems through non-covalent interactions to reduce solvent use and improve reaction control.

- **Combinatorial Green Chemistry:**

Quickly producing many compounds with minimal resources and waste.

- **Safer Oxidation Reagents and Catalysts:**

Developing alternatives that avoid toxic heavy metals.

- **Biometric (Bio-based) Multifunctional Reagents:**

Using natural molecules that can perform multiple reaction roles.

In pharmaceuticals, green chemistry is becoming an important trend because it helps design safer chemicals and manufacturing methods. It reduces harmful effects on health and the environment while supporting sustainable production. Chemists focus creating effective, eco- friendly products that use hazardous materials, produce less waste, and require less energy.

Benefits of Green Chemistry

- Turning waste into valuable products.
- Reducing or eliminating toxic chemicals.
- Using environmentally safe solvent systems.
- Developing eco-friendly chemicals and materials.
- Designing industrial processes that avoid health and safety risks.
- Studying the environmental and toxic impacts of biomass-based processes.

11. CONCLUSION: -

Green chemistry has become an essential part of modern pharmaceutical development because it focuses on reducing pollution, saving resources, and making drug production safer for people and the environment. By applying the 12 principles of green chemistry, the pharmaceutical sector can use fewer toxic chemicals, produce less waste, and improve overall process efficiency. Practices such as using safer solvents, biocatalysis, renewable raw materials, solvent recycling, and continuous-flow technology show that industries are actively moving toward greener methods. Green analytical techniques are also helping laboratories reduce chemical consumption and energy use.

Although many improvements have been made, full adoption of green chemistry in pharmacy still faces challenges like high implementation cost, lack of trained professionals, and strict regulatory requirements. However, continuous research, government support, and industry collaboration can overcome these barriers. Overall, green chemistry provides a sustainable pathway for developing future medicines that are safe, affordable, and environmentally friendly.

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