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REVIEW ARTICLE

SUSTAINABLE STRATEGIES FOR DEVELOPMENT OF GREENER PHARMACEUTICAL PRODUCTS AND EXCIPIENTS

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ABSTRACT

The pharmaceutical business and its worldwide supply chain play a significant part in the healthcare system, but it also has notable repercussions for the environment. Drug manufacture and transportation are major factors to the pharmaceutical industry's carbon footprint. Like other manufacturing sectors, the pharmaceutical business contributes improve the sustainability of its operations. The current review focuses on sustainable strategies of pharmaceutical companies in order to achieve the greener goals. The field of chemistry known as "green chemistry," often called "sustainable chemistry," focuses on designing and improving goods and processes to reduce or eliminate the usage and production of hazardous materials. Sustainable hazardous waste management is critical for a safe, clean, and environmentally friendly environment and public health. The paper reviews newly developed management approaches, waste-to-energy conversion processes, and treatment technologies, as well as their applicability, advantages, and limitations. The extensive analysis presented in this article will assist in the formulation of cost-effective and environmentally friendly long-term development goals, as well as a number of projects to improve the pharmaceutical industry.

Keywords: Green chemistry, Sustainable strategies, Pharmaceutical waste management

INTRODUCTION

Sustainability and sustainable development goals

Defining the Meaning of Sustainability Despite the proliferation of health literature on sustainability, there is little consensus on how to define it. Sustainability was described with terms such as "continuation", "maintenance", "sustainability", "adoption", "contract", "relational", "adoption", "continuity", "integration", "long-term" and "contact". Fewer scholars generally define sustainability as "the maintenance of health benefits over time", USAID defines it as "the ability to maintain program services at a level that ensures ongoing prevention and treatment of health problems after significant financial, administrative and technical assistance from an external donor has ended. " Other researchers focus only on program components and define sustainability as "the continued use of program components."[1]

How pharmacy is connected with sustainable development goals as per WHO?

The Sustainable Development Goals (SDGs), officially known as Transforming our world: the 2030 Agenda for Sustainable Development is a set of 17 "Global Goals" [2], which in brief are as follows **(Fig. 1):**

Pharmaceutical Industry and Health / Cities / Environment

To meet the goals set out at the COP 26 conference in 2021, and recently confirmed at COP 27, nations throughout the world have set aims to achieve net zero carbon emissions and a brighter society by 2050. To help with this effort, energy-intensive industries, such as the pharmaceutical industry, are being pushed to change practices and set their own ambitious targets to futureproof operations. The three goals are directly linked with the pharmaceutical sectors which includes good health and well-being (SDG 3), sustainable cities and communities (SDG 11) and climate action (SDG 13). While some effects of climate change, such as continued sea level rise, cannot be reversed, "strong and sustained reductions in emissions of carbon dioxide (CO2) and other greenhouse gases (GHGs) would limit climate change" going forward, according to the latest Intergovernmental Panel on Climate Change report released in August 2021. Like other manufacturing sectors, the pharmaceutical business contributes improve the sustainability of its operations. To see how the sector

Figure 1: Sustainable Development- 17 "Global Goals"

is fairing, we reviewed pharma companies reporting environmental, social, and governance (ESG) scores. The Green Chemistry Working Group of the IQ Consortium initially met with the FDA in 2012 to identify prospects for boosting green chemistry. As a significant delivery device partner for pharmaceutical firms, one must also optimize their own processes. The following shows progress made to far towards being more sustainable - including examples from journey - and highlights areas where improvement has been missing thus far. [3]

GREEN CHEMISTRY AND SUSTAINABILITY

According to one scientist in US, Pharmaceuticals, the notions of green chemistry and sustainability have been widely embraced in the pharmaceutical business over the past 15 years, in the routine creation of greener API processes for all projects via innovative chemical research and new technologies. However, other scientists emphasises that more ways besides green chemistry principles should be considered to achieve true sustainability, such as designing an effective waste management strategy at the end of the process. The field of chemistry known as "green chemistry," often called "sustainable chemistry," focuses on designing and improving goods and processes to reduce or eliminate the usage and production of hazardous materials. Environmental chemistry and green chemistry are not the same thing. The former focuses on how chemistry affects the environment and how environmentally friendly sustainable practices may be developed (such cutting back on the usage of non-renewable resources and developing pollution control measures). The latter focuses on how certain harmful or poisonous compounds affect the environment.[4]

The following is a list of the twelve guiding concepts for green chemistry that were proposed in 1998 by American chemists Paul Anastas and John Warner **(Fig. 2):**

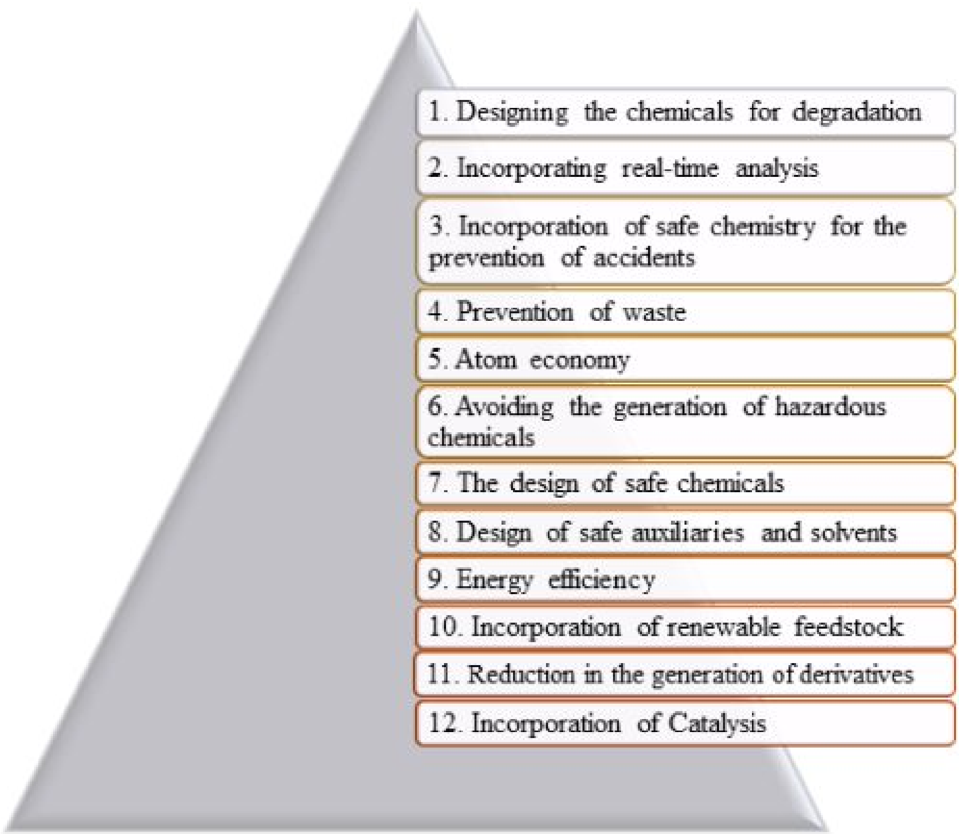


Figure 2. 12 key principles of green chemistry

1. **Designing the chemicals for degradation:** When constructing a chemical product to perform a certain purpose, care must be taken to ensure that the chemical is not an environmental contaminant. This may be accomplished by ensuring that the chemical degrades into non-toxic compounds.

2. **Incorporating real-time analysis:** It is necessary to build processes and analytical techniques to the point where they can provide real-time data for their monitoring. As a result, the process may be stopped or controlled by the people involved before harmful or dangerous compounds are created.

3. **Incorporation of safe chemistry for the prevention of accidents:** It is critical to ensure that the compounds used in chemical processes are safe to use while developing them. This may aid in the prevention of industrial hazards such as explosions and fires. This may also assist to create a safe environment around for procedure to take place in.

4. **Prevention of waste:** In any circumstance, it is preferable to avoid the creation of waste materials rather than to clean up garbage after it has already been generated.

5. **Atom economy:** Green chemistry-based synthetic processes must include all raw materials into the end product to maximise consumption. Strict adherence to this is necessary to reduce the amount of trash produced by any kind of procedure.

6. **Avoiding the generation of hazardous chemicals:** To prevent the certain of some poisonous compounds that harm human health, reaction and processes that include the synthesis of such molecules must be optimised.

7. **The design of safe chemicals:** Chemical goods must be non-toxic to persons and the environment when designed to perform a certain purpose. Developing chemical goods to achieve a goal requires procedures to assure health and safety for humans and the environment.

8. **Design of safe auxiliaries and solvents:** The use of auxiliaries in processes should be minimized and optimized to minimize hazards, even when necessary.

9. **Energy efficiency:** The amount of energy consumed by the process must be decreased as much as possible to the best of its capacity.

10. **Incorporation of renewable feedstock:** It is critical that the use of renewable raw materials and components be prioritised over the usage of non-renewable ones.

11. **Reduction in the generation of derivatives:** Minimizing the unnecessary use of derivatives is crucial as they often require additional reagents and chemicals, leading to excess waste generation.

12. **Incorporation of Catalysis:** It is critical to encourage the usage of such catalysts and catalytic reagents in order to reduce the energy demands of the chemical reactions that occur throughout the process.[5]

Impact of medicines on environment and connection with health

Medicines have a significant role in both human and animal illness treatment and prevention. However, due to the nature of medicines, they may have unforeseen consequences for animals and microbes in the environment. Although the side effects on human and animal health, are explored in toxicology and safety studies, the potential environmental repercussions of pharmaceutical manufacturing and usage are less well recognized and have only lately become a research focus of interest [6]. Some of the impacts of various chemicals are widely accepted, most notably veterinary anthelmintics and antibacterial treatments, however there are many other substances that can affect organisms in the environment. Furthermore, breakdown products and the mixing of multiple physiologically active chemicals may have unforeseen environmental impacts. As people can observe, it is critical that we work together to keep all drugs out of the environment, where they might hurt other animals and potentially endanger us.[7]

SUSTAINABLE STRATEGIES: GREEN CHEMISTRY AND PHARMACEUTICAL MANUFACTURING

Drug design tries to optimise the pharmacological benefits for a specific target while minimising the drug molecule's toxicological consequences. The purpose of pharmaceutical process development is to offer efficient manufacturing conditions that eliminate or minimise toxicologically active contaminants.[8]

The ICH guideline for residual solvents in medicines divides solvents into three classes, from toxic or carcinogenic solvents to class 3 solvents with little toxicologic potential.

- Avoiding the use of hazardous solvents and process conditions that result in impurities coincides with the green chemistry idea of 'choose synthetic methods employing nontoxic substances' as well as regulatory requirements such as those outlined in the ICH.
- The use and definition of green solvents from a green chemistry ensure patient safety.
- The development of APIs and other drug components with less environmental impact is a component of the solution to the issue of API residues in the environment.
- However, a reduction of the impact of pharmaceuticals on the environment can be addressed

The proposed GREENER concept, including a "benign by design" approach, takes the natural environment as well as the patient into account.

Transition to eco-friendly packaging

In contrast to non-recyclable (or difficult-to-recycle) packaging such as plastic bags, composite chip bags, polystyrene clamshells, sustainable packaging generates little, wrappers or no waste. Eco-friendly items, rather than ending up in a landfill or the ocean, either decompose or can be recycled. They are shifting away from old, potentially hazardous packaging materials and towards more sustainable options. But how do they do it? Let's take a look at green packaging in pharmaceuticals.[9]

The following are the most common types of sustainable packaging:

a) **Compostable -** Compostable packaging is manufactured from materials that degrade in the environment without releasing hazardous chemicals. [10]

b) **Biodegradable -** Biodegradable packing materials degrade in the environment as well. Biodegradable materials which require a particular environment

c) **Recyclable -** Recycling materials can be gathered and remanufactured into new goods.

Many regularly used packaging materials are potentially recyclable, but end up in trash because they are too complex and energy-intensive for standard recycling streams to handle.[11]

Here are a few ways that companies can reduce the environmental impact of their packaging:

- Reduce the use of packaging materials.
- Use recycled materials
- Implement biodegradable or compostable materials
- Optimise packaging design
- Use eco-friendly transportation
- Encourage recycling

Improve waste management

Pharmaceutical wastes may be produced by a range of activities in the health care system, including the use of syringes, and are not limited to intravenous (IV) preparation. In general, pharmaceutical waste may consist of personal medications, Waste material chemotherapy drug residues, excess drugs, Containers with hazardous waste drugs, Open containers of drugs that cannot be used, Drugs discarded; and Contaminated garments, absorbents, and spill cleanup material, Expired medications, Environmental groups, law enforcement agencies, government agencies, and waste management organisations are all collaborating to avoid pharmaceutical contamination.[12]

Strategies for Hazardous Waste Management for Waste minimization

Incineration

Incineration is a waste disposal process that burns solid organic waste to create residue and gaseous by-products. This method is ideal for solid waste and water management residue disposal. Solid waste is reduced by 20–30% using this strategy. Incinerators and other high-temperature waste treatment facilities are called "thermal treatment". Waste incinerators create heat, gas, steam, and ash. Industrial trash incineration is far larger than residential garbage incineration. It disposes of solid, liquid, and gaseous waste. Some hazardous garbage may be disposed of this manner (For example, biological medical waste). Incineration is controversial due to gaseous pollution. Burning unsuitable materials like pressurised gas canisters, reactive chemical waste, halogenated chemicals, polymers, mercury, and radiography waste requires complex incineration designs with air pollution control devices, secure landfills, skilled operators, and high investment costs.[13]

Autoclaving

In autoclaving, pathogens are killed by putting the Biomedical waste (BMW) in a pressure vessel with saturated steam that comes into direct contact with it. This happens for a long enough time and at a high enough temperature. The Biomedical Waste Rules say what the autoclaves must have in terms of temperature, pressure, and reside time in order to safely disinfect. Before being put in an autoclave, BMWs need to be shred to a good size, which is a process that would break down often. When you use an autoclave, you make waste that can be dumped in the ground with regular trash. It creates a stream of wastewater that needs to be disposed of properly. Autoclaves need qualified technicians to run, and they cost about the same to buy and run. No matter how helpful it is, autoclaving is not good for getting rid of human or animal body parts, chemicals, or pharmaceutical waste. [14]

Microwaving

An electromagnetic field applied to the BMW causes the liquid in the waste to vibrate and heat up, eliminating the pathogenic components by conduction. If the UV light reaches the waste material, this approach is effective. BMWs need shredding to an appropriate size and humidification before to microwaving. Microwaving is incompatible with human anatomical, animal, chemical, or pharmaceutical waste, as well as big metal components. Microwaving generates garbage that may be landfilled with municipal rubbish. The benefits of this treatment system include low electrical energy requirements and no need for steam. The downsides include the necessity for skilled personnel and the frequency with which shredders fail. This technique requires a moderate investment and running expenditures.[14]

Deep burial

A pit or tunnel should be excavated around two metres deep. Fill half of the hole with garbage and cover with lime up to 50 cm from the surface before filling with soil. When adding garbage to the pit, always cover it with 10 cm of soil. According to the Biomedical Waste Rules, Deep burial is only an option in remote locations without access to centralised treatment facilities, with prior clearance from the prescribed the law enforcement officials. Animals must not have access to burial grounds. Covers made of galvanised iron or wire mesh can be utilised. The pits should be set far enough away from population to prevent surface or ground water pollution. The groundwater table should be at least six metres below the deep burial pit's lowest level. The region should be resistant to flooding and erosion. The location of the deep burial site must be approved by the appropriate authorities, such as the CPCB/SPCB or the District Pollution Control Board Office. The institution must keep a record of all trenches utilised for deep burial. The greatest advantage of deep burial is that harmful substances do not travel straight away to the ground surface.[15]

Chemical disinfection

In the context of a health care facility, chemical disinfection is most effective when used to the treatment of liquid wastes such as blood, urine, faeces, or sewage systems. Strong oxidants, such as chlorine compounds, ammonium salts, aldehydes, or phenol compounds, are added to the environment in order to make pathogens inert. Additionally, the length and duration of contact between the waste and the disinfectant, as well as the kind and amount of chemical that is used, are all factors that impact the success of the disinfection process.[14]

Secure land filling

Landfilling solid BMWs at a hazardous waste facility is secure. Pharmaceuticals, cytotoxic medications, solid chemical waste, and incinerator ash must be disposed of in safe landfills under the Biomedical Waste Rules. Burying garbage in landfills is still common in most nations. Underused quarries, mining voids, and borrow pits were utilised for landfills. A properly constructed and managed landfill can safely and affordably dispose of rubbish. Wind-blown rubbish, vermin recruitment, and liquid leachate may result from older, poorly designed, or poorly managed landfills. When organic waste decomposes anaerobically, landfills release gas (mainly methane and carbon dioxide). A greenhouse gas, this gas destroys surface plants and generates odours. Modern landfills use clay or plastic liner to contain leachate. Ordinary rubbish is compacted and coated to increase density and prevent bugs (such as mice or rats). Landfill gas extraction systems are implemented at numerous landfills. Gas from landfills is pumped via perforated pipes and flared or burnt in gas engines to generate electricity.[16]

Waste immobilization

a) Encapsulation

Encapsulation is extremely useful for disposing of objects that are sharp and other materials which may become sharp. It is also excellent for the disposal of pharmaceutical residues and some dangerous substances. One key advantage of the strategy is that it reduces the risk of scavengers accessing dangerous medical waste. Encapsulation is the process of solidifying medications in a plastic or steel barrel. Drums should be clean and have not contained explosives. Most hazardous wastes may be mixed into a waste-cement system, which contains 75% solid and semi-solid medicines and the remaining cement, cement/lime, plastic foam, or bituminous sand. Cut the drum lids apart and bend them back to facilitate filling. Avoid cutting your hands while putting drugs into drums. After 75 percent of the barrels have been filled, a 15:15:5 (by weight) mixture of cement, lime, and and water is added to fill them completely. To make transporting the drums easier, place them on pallets, which may then be loaded onto a pallet mover. [17]

b) Inertization

Inertization is a process where pharmaceuticals are removed from packaging materials, pills are extracted from blister packets, and a homogenous slurry of water, cement, and lime is formed. Due to the possibility of dust, workers must wear protective clothes and wear masks. The paste is then delivered in liquid form to a landfill by a concrete mixer truck and decanted into regular municipal garbage. The paste subsequently solidifies and disperses throughout the municipal solid garbage. The procedure is quite affordable and may be performed using simple equipment. The primary needs are a grinder or road roller to smash the medicines, a concrete mixer, and cement, lime, and water supply.[16]

Sewer

Some liquid medications, such as syrups and intravenous (IV) fluids, may be diluted with water and disposed into sewers in modest amounts over time without causing severe public health or environmental problems. Small amounts of well-diluted liquid medications or antiseptics may also be flushed down fast running watercourses. In cases when sewers are in disrepair or have been damaged by conflict, the aid of a hydro geologist or sanitary engineer may be necessary.[18]

Key contributing factors associated with active pharmaceutical ingredients

Dynamic drug fixings (APIs) can enter the indigenous habitat because of assembling, use, as well as removal, making public affected by about possible ecological hazards. One disadvantage of estimating ecological data sources in view of utilization inside a nation is that adherence to Programming interface treatment, especially for long haul treatment, is around half in big league salary nations and much lower in lower-pay economies. Albeit this action may consequently misrepresent Programming interface use, a significant number of these unused APIs can in any case be discarded in a way that will ultimately bring about ecological corruption. [19]

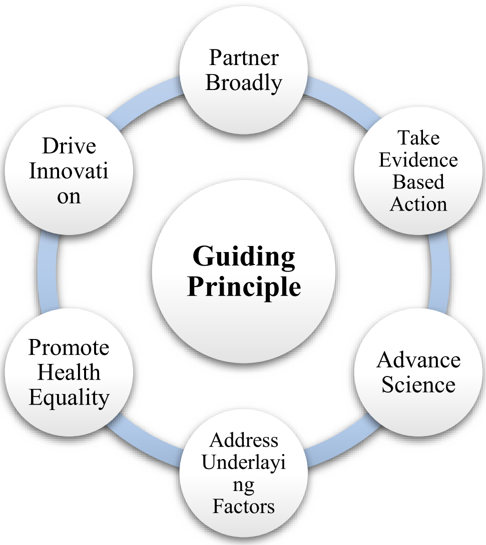
Factors influencing consumption patterns of active pharmaceutical ingredients

1. Disparities in disease loads
2. Healthcare policy
3. Cost-effectiveness of active pharmacological substances
4. Self-medication and excessive prescribing
5. Antibiotics and other active pharmacological substances used in veterinary medicine
6. Active therapeutic ingredient consumption rates
7. Non-traditional active pharmacological ingredients: complementary and alternative medicine's contribution
8. Receiving environments

Reducing toxicity in drugs / Green Toxicology for the early assessment of environmental safety

One of the most challenging parts of creating safer products and processes is minimizing toxicity while maintaining functionality and efficiency **(Fig. 3).** To achieve this goal, you need to understand not only chemistry, but also the principles of environmental science and toxicology. Highly reactive chemicals for the production of products because they are very effective in carrying out molecular changes that are more prone to react with unexpected biological targets, both ecological and human, causing unexpected negative effects. Even the most experienced molecular magician runs into trouble without a full toolbox if they don't understand the basic structure hazard relationship.

Drug toxicity is caused by a variety of physiological parameters, including age, dose-time correlation, exposure time, dietary position, gender, sex, and hormonal circumstances. Overdose deaths can be avoided.[20]



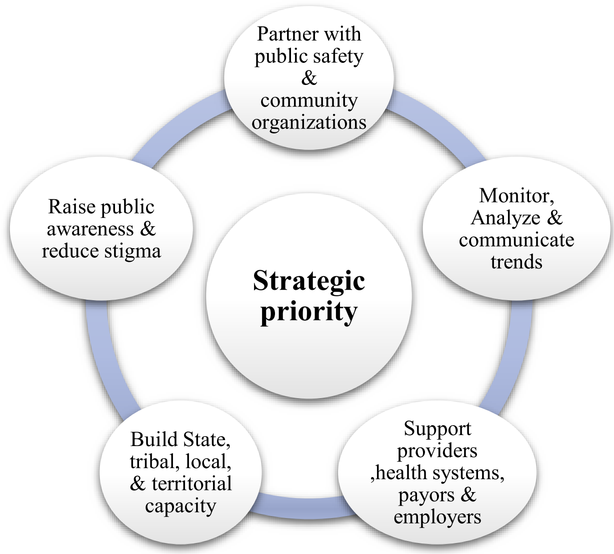


Figure 3. Measures to prevent overdoses and substance use-related harms.

Educate the public on how to use and dispose of medication

Household Waste Disposal Recommendations from the Food and Drug Administration.

- Remove pills from original containers,
- Mix with unwanted substance
- Place combination in disposable container with a cover and seal,
- Remove any identifying information from the empty original container,
- Throw away the sealed mixture and the empty original container

There is a lot of waste in the pharmaceutical industry, but it doesn't have to be that way. Every pharmaceutical firm, manufacturer, and facility can help to make pharma greener by adopting a proactive attitude and implementing sustainable solutions. [21]

CONCLUSION

Green chemistry is becoming more and more popular all over the world. Not only does green chemistry solve many environmental problems, but it also creates high quality products with minimal harmful material residues. When we look at the overall situation of the pharmaceutical industry, and the challenges we face, including environmental concerns, high-cost products, and many more, we can say that green chemistry is a revolutionary way to improve living standards while reducing environmental issues. Green chemistry is good for the environment and good for the economy. Green chemistry will transform conventional pharmaceutical companies into sustainability companies.

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