

Programming the fate of medicines: An eco-by-design strategy for zero pharmaceutical residues



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Abstract:

Pharmaceutical residues are a serious threat to the environment, biodiversity, and human health. Traditional pharmaceutical research & development is inherently unsustainable, as it does not consider the environmental impact of drug design, synthesis, packaging, and disposal. The proposed solutions, Eco-by-Design Pharmaceuticals and Programming the Fate of Medicines, address the issue from multiple angles. At the molecular level, the design utilizes cleavable linkers that are stable in the shelf-life of the drug but are easily degraded in water, thus minimizing the environmental footprint. Green chemistry approaches, including catalysis, mechanochemistry, continuous flow, and solvent recycling, help reduce the ecological impact of drug synthesis. The use of chitosan, cellulose nanocrystal composites in packaging reduces plastic waste and ensures the stability of the drug during transportation. Finally, the use of biochar beds made from agricultural waste to trap and detoxify pharmaceutical residues is an excellent example of a sustainable end-of-life solution.

Keywords: Pharmaceutical residues, Sustainability, Eco-by-design, Bio-cleavable drugs, zero waste

1. Introduction

For a long time, people making new medicines focused on how well they work and how safe they are for patients. But they didn't think as much about how these medicines affect the environment. When medicines get into the soil and water, they can cause big problems like pollution and help create germs that are hard to kill with antibiotics. (1) The reason medicines work well in our bodies is because they are strong and don't break down easily. But this also means they don't break down easily in the environment, which can cause more problems (1)

Even trace amounts can upset aquatic ecosystems, with low-level residues shown in studies to contribute to ecological stress (2). This highlights the deficiencies of conventional

pharmaceutical development, where design, synthesis, manufacturing, packaging, and disposal are all done separately without regard for their combined environmental footprint (3). Medications that safeguard human health can simultaneously generate unintended ecological pressures (3).

In order to meet these challenges, sustainability must begin at the design stage rather than after contamination. This review describes the programming of the fate of medicines; a design-to-disposal framework that integrates bio-cleavable drug architecture, green synthesis, intelligent manufacturing, sustainable bio-packaging, and circular remediation (4).

2. Programming the fate of medicines through molecular design

The fate of medicines in the environment is determined at the design stage since Eco-by-Design Pharmaceuticals aims to develop medicines with reduced environmental impact while providing the desired therapeutic function (5). The principles of Green Medicinal Chemistry should be integrated into the design to ensure that pharmaceutical activity occurs with minimal negative effect on the environment (6).

The most promising strategy is based on the design of bio-cleavable drugs that can be easily degraded after use while providing the required therapeutic effect before entering the environment. It is possible due to the use of targeted linkers that can be cleaved using particular enzymes resulting in the formation of pharmacologically inactive molecules (7). Ester, hydrazone, carbonate, peptide, and disulfide linkages can be used to develop drugs degradable in different environments.

The key challenge associated with the design of degradable drugs is the need to ensure their stability during use while allowing their easy degradation after eliminating the pathology symptoms. The appropriate choice of linkers and enzymes responsible for drug degradation allows addressing this challenge and designing a medication degradable in specific environments, such as water, and not degradable in the human body (8). Table 1 depicts the various bio-cleavable linkers.

Table 1. The list of bio-cleavable targeted linkers

Linker	Cleavage mechanism	Stability	Environmental degradation	Pharmaceutical applications	Sustainability benefit
Ester	Hydrolysis (aqueous)	Moderate	Rapid	Prodrugs, biodegradable APIs	Fast breakdown in water
Carbonate	Enzymatic hydrolysis	Moderate	Efficient	Drug delivery carriers	Biocompatible by-products
Hydrazone	Acidic hydrolysis	Stable in neutral	Controlled	Targeted release systems	Reduced persistence

Peptide	Protease cleavage	High	Selective	Peptide drugs, carriers	Natural degradation
Disulfide	Oxidative cleavage	Stable in plasma	Rapid in oxidative media	Anticancer prodrugs	Environment-t triggered



Figure 1. Framework for programming fate of medicines

2.1. Translating Design into Practice

Sustainable molecular design requires translation into practice via green synthesis and intelligent manufacturing to make sure that the pharmaceutical industry remains eco-friendly. Although design programs the future of medicines, it is manufacturing that makes them sustainable. Green organic synthesis lies at the heart of the process, being focused on such a crucial concept as atom economy, thus minimizing waste (9). In addition, catalysis allows one to make processes more selective, cutting down on energy and undesirable byproducts (9).

Other innovative approaches to make the production of pharmaceuticals greener include mechanochemistry, which involves the mixing of compounds without a solvent, and flow chemistry that is used to make continuous manufacturing processes (9). Combined with continuous manufacturing, they make processes controlled and optimized, thus removing risks.

In addition to that, the use of Process Analytical Technology and Quality by Design makes it possible to monitor production and build sustainability into products (10). The development of new approaches to pharmaceutical manufacturing using artificial intelligence also contributes to the industry's sustainable development by being able to predict the most efficient processes

and conditions (10). Finally, the implementation of solvent recovery and zero-waste manufacturing is vital for pharmaceuticals' sustainability, as it allows one to recover expensive solvents and not impact the environment unnecessarily. Each step of the way, from design to manufacturing, pharmaceutical products are made to be sustainable and beneficial for health without compromising the environment.

2.2. Extending Sustainability beyond Manufacturing

Pharmaceutical sustainability should not be limited by the boundaries of manufacturing. The environmental impact of the drugs should be considered at later stages of consumption and even after disposal. Typically, traditional petroleum-based plastics used for packaging have significant environmental consequences after disposal. Materials such as chitosan provide an excellent alternative because they are biodegradable and possess antimicrobial properties, thus addressing two critical issues: the excessive plastic waste in the environment and multidrug resistance (11). Moreover, cellulose nanocrystals offer a sustainable option for wrapping and packing medications due to their mechanical properties, flexibility, and biodegradability (12). The combination of chitosan and cellulose nanocrystals in composite bio-films offers a platform for pharmaceutical packaging with improved properties.

Another significant advantage of pharmaceutical packaging is the potential to use smart wraps that can indicate the expiry date of the medicine. Besides, the use of such technology can also prevent the wastage of pharmaceutical products due to improper storage and ensure patient safety. However, even after use, pharmaceutical packaging can negatively impact the environment because some of the compounds can be hazardous in landfills. Indeed, most Active Pharmaceutical Ingredients (APIs) are poorly degraded in various environments and accumulate in it, severely impacting the waste treatment plants, wildlife, and even human health. For example, API residues disrupt essential microbial processes and threaten aquatic organisms with bioaccumulation. At the same time, antibiotics facilitate the development and dissemination of antibiotic resistance genes amongst bacteria (13).

Therefore, it is evident that the impact of pharmaceutical products should be considered even after their use. Thus, it is critical to ensure sustainable practices both in manufacturing and post-consumer use to minimize the impact on human health and the environment. Table 2 shows the comparison of traditional and sustainable packaging.

Table 2. Conventional vs Sustainable pharmaceutical packaging difference

Particulars	Conventional packaging	Sustainable packaging	Benefits to environment
Material	Petroleum based plastics	Chitosan, nanocellulose, biopolymers	Biodegradable, renewable resources
Barrier properties	High but non degradable	Comparable with eco-friendly composites	Maintains drug stability, reduces waste
End of life fate	Landfill accumulation	Compostable or recyclable	Lower ecological footprint

Functionality added	Passive containment	Smart indicators, antimicrobial films	Reduced drug wastage, improved safety
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2.3. Closing the loop

Pharmaceutical sustainability requires a cradle-to-grave approach; thus, the industry should create ways to reuse or remove drug residues. Medicine take-back programs can ensure that the compounds are disposed of correctly instead of being flushed down the drain (14). The pharmaceutical residues can then be treated using agricultural biochar to remove pollutants before they reach the environment (15). More sophisticated technology, such as advanced oxidation processes, photocatalysis, and enzymatic treatments, can break down the contaminants into simpler, harmless molecules as shown in Table 3.(16,17). This way, the loop of pharmaceutical waste is closed, and the medicines are taken away from the environment after use.

Table 3. The end-of-life circular technologies

Technology	Principle	Advantages	Limitations	Best Application
Medicine Take-back	Safe collection of unused drugs	Prevents improper disposal	Requires public participation	Community pharmacies, hospitals
Agricultural biochar	Adsorption of pollutants	Low-cost, scalable	Limited for highly soluble APIs	Soil and water remediation
Advanced oxidation	Hydroxyl radical degradation	Rapid breakdown	Energy intensive	Wastewater treatment plants
Photocatalysis	Light-activated mineralization	Complete degradation	Catalyst stability issues	Aquatic effluent treatment
Enzymatic degradation	Biological cleavage of molecules	Selective, eco-friendly	Slow kinetics	Targeted pharmaceutical residues



Figure 2. The design-to-disposal circular framework

3. Future Prospects

With the future prospects, pharmaceutical sustainability will be achieved through the development of AI-designed biodegradable drugs and the use of carbon-neutral production technologies to ensure therapeutic stability while promoting environmental sustainability (18,19). Smart biodegradable packaging will also contribute to sustainability by minimizing waste and enhancing shelf-life (20). Also, advanced regulations and continued research on biodegradable designs are critical factors that will promote pharmaceutical sustainability.

4. Conclusion

Drugs should be designed to be effective and safe for the environment by incorporating the principles of eco-by-design, using green synthesis, and implementing strategies to mitigate the threat of drug resistance, as well as designing sustainable approaches to packaging and disposal to minimize the impact on the environment. Design to-disposal concept makes sure that drugs are developed and used in a way that helps both patients and environment.

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