How to foster the Circular Economy within the Pharmaceutical Industry? A research framework proposition

Simon MASSOT[1,2], Duc-Nam LUU[1], Claus-Jürgen MAIER[3], Nicolas MARANZANA[1], Améziane AOUSSAT[1]

[1] Arts et Métiers Institute of Technology, LCPI, HESAM Université, 151 boulevard de l'Hôpital, 75013 Paris, France
[2] Sanofi, 82 avenue Raspail, 94250 Gentilly, France
[3] Sanofi, Industriepark Höchst, 65926 Frankfurt am Main, Germany
simon.massot@ensam.eu

Abstract. Pharmaceutical industries play an integral role in our society as their primary purpose is to provide products that enhance human health and well-being. Due to its intrinsic activities, the impact of the healthcare sector on the environment is consequent. However, the preservation of our environment is a prerequisite to ensure human health resilience. The circular economy (CE) is a model of production and consumption aimed to preserve the environment. The CE principles, such as "Reduce, Reuse, Recycle" [1,2] are required in an expanding world where resources are limited [3], and the generation of waste increases each year. Considering the size of the pharmaceutical sector in the global economy and the fact that less than 10% of our economy is circular [4], it is essential to implement the concept of circularity to limit the tremendous resource consumption. Nevertheless, most of the work that has been done in this area focuses on a few specific steps of drug and medical device development processes [5,6], creating room for implementation opportunities. The goal of this paper is to provide a mapping of the research that has been done in the field of CE, related to the pharmaceutical sector. As circularity is driven by design, this paper focuses on the whole value chain of pharmaceutical products, from raw material extraction to the end of life. The findings of this study are categorized regarding product life-cycle steps. This allows the identification of current research trends and opportunities for future research and potential circular solutions.

Keywords: Circular Economy, Pharmaceutical Industry, Design Process, Lifecycle

1 Introduction

The industrial revolutions and the development of human society have led to important consequences for our environment, such as the depletion of natural resource. The negative impacts of our society have been growing exponentially for many years and are considered as the biggest challenge of the 21st century [7]. The concept of

planetary boundaries, established in 2009, defines environmental limits in which humanity can operate safely and depicts the emergency of the situation [8]. Pharmaceutical industries play an integral role in our modern societies due to their intrinsic purpose which is developing medicines and medical devices to prevent, heal, cure, and diagnose diseases to maintain the population's health and well-being. However, the production of drugs is responsible for important pollution and negative environmental impacts.

The Circular Economy (CE) is a model of production and consumption that aims to implement environmental sustainability and its principles into organizations. Integrating circularity into an organization means continually reusing products, materials, and resources whenever possible [9]. In opposition to a linear business model "take-make-use-dispose", the CE's purpose is to create loops in the product life cycle, to retain the value of the resources. Today, only 7,2% of our world is considered circular, and the majority of organizations work in a linear economy [4]. The CE is a promising concept that could help pharmaceutical companies in achieving sustainability goals and improve their environmental performances. Nevertheless, since the purpose of circularity is to reduce the environmental footprint of products, circularity must be taken into account across the entire product life cycle using a multicriteria approach, such as the eco-design one.

This paper proposes a mapping to categorize the existing literature on the CE within the pharmaceutical industry regarding the several life cycle steps of medicines. The first parts of this paper introduce the CE, and the pharmaceutical industry. Then, the literature analyzed is presented and, a mapping is proposed which allows the identification of the main research axis for CE in the healthcare sector, and future potential opportunities.

In conclusion, the goal of this paper is to answer to the following research question: *How can the CE research for the pharmaceutical sector be classified to foster further research and opportunities?*

2 Circular Economy

2.1 Definition and principles

The CE is a concept born in the middle of the 1990s which integrates different principles and concepts. For many authors, the CE is frequently depicted as an easier way to allow the operationalization of sustainable development into businesses [1]. Therefore, the CE is a trending concept as the number of publications increased significantly in the last few years. Numerous organizations have proposed their definition and most of them are based on the same principles. Kirchherr et al., conducted a study of 114 definitions of the CE, from 2005 to 2017 [1]. A systematic analysis of the definitions allowed the authors to demonstrate that even if most of the definitions are different, some common points can be highlighted. First, the fact that in opposition to a linear economy "take-make-use-dispose", the CE aims to have better management of resources throughout the life cycle of systems and to retain the value of products and materials. Second, the CE principles aim to generate loops in the product life cycle. There are three types of loops: short, medium, and long, and they do not present the

same benefits or consequences for the environment. Indeed, the shorter the loop is, the better to keep the value of the material/product. Hence, it is more interesting to reuse a product than to recycle it.

The following definition from the Ellen MacArthur Foundation (EMF) was established in 2013 and is well recognized among peers and in the industry [2]: "*A systems solution framework that tackles global challenges like climate change, biodiversity loss, waste, and pollution. It is based on three principles, driven by design: eliminate waste and pollution, circulate products and materials (at their highest value), and regenerate nature [...]*".

Transitioning to a CE will be systemic, deep, and transformative. It is not only recommended but it is a crucial part of the transformation of industries to improve their environmental performances [10]. Even the EU made a proposal for a new Eco-design for Sustainable Products Regulation, published on 30 March 2022, that is the cornerstone of the Euro-pean Commission's approach to more environmentally sustainable and circular products [11].

2.2 Review of existing CE frameworks

Since the apparition of the CE and its numerous definitions and interpretations, several frameworks have been proposed and aim to help organizations structure the integration of the CE within their business models.

Table 1. Example of the most common CE frameworks

3R [1]	Most common conceptualization of the "how-to" of the CE Several adaptations proposed in the literature (4R, 6R, etc.) • Reduce, the consumption of natural resources/materials • Reuse, the discarded product by another consumer • Recycle, process materials or products to obtain the same or lower quality
9R [5]	One of the adaptations of the 3R framework Additional principles: refuse, rethink, repair, refurbish, remanufacture, repurpose. Emphasizes the differentiation between short, medium, and long loops to help the identification of specific levers for practitioners
Butterfly diagram [2]	It represents continuous flows of materials in a CE. Those flows are divided into biological and technical cycles. The cycles are divided into several loops, the inner loops refer to short loops, and the larger ones to long loops.
ReSOLVE [12]	Translation of the CE principles into six actions: Regenerate, Share, Optimize, Loop, Virtualize, and Exchange. Each action represents a major circular business opportunity. Actions can be considered individually but a compounding effect can appear if many of them are addressed.

Many CE frameworks exist in the literature as a basis for CE actions, such as the ones proposed by the circle economy organization. However, the frameworks presented

previously represent some of the most important frameworks and their associated concepts. The use of such CE frameworks within the pharmaceutical industry is an opportunity to reduce the environmental burden generated by this sector.

3 The pharmaceutical industry

This section aims to give an overview of some specificities of the pharmaceutical industry which help to understand why a focus on this specific sector is proposed, and why it is important to foster CE studies.

3.1 Specificities of the pharmaceutical industry

The pharmaceutical industry is a highly regulated industry, which needs to comply with numerous strict standards and regulations. As the purpose of this industry is to provide the population with medicines to protect and preserve their health, the developed products need to be aligned with high-quality and safety standards. Those standards might differ from one country to another because many regulations are established at a national level. These regulations are considered in a singular development process and potential environmental levers were identified as described by Luu et al., 2022 [13].

3.2 Environmental impact of the pharmaceutical sector

The pharmaceutical industry plays an integral role in our modern societies. However, as with any human activity, pharmaceutical companies are responsible for important environmental impacts. Several studies focused on this topic and assessed the impact of this sector on the environment regarding different aspects such as climate change, biodiversity, natural resources, and so on. According to Eckelman who has led numerous studies on the impact of the healthcare sector, the pharmaceutical industry contributes to approximately 4.5% of worldwide global greenhouse gas emissions [14]. Not only do those emissions pollute our environment, but they are also responsible for the apparition of diseases into the population [15].

Due to their intrinsic nature, Active Pharmaceutical Ingredients (API) and their metabolites have tremendous impacts on our ecosystems. A large-scale study has been conducted across the world, analyzing the presence of 61 API in more than 1000 sampling sites and more than 250 rivers, and has shown that the presence of those API is important and increase each year [16]. The global population growth coupled with the pollution of our environment contributes to an increasing number of diseases internationally, which can have a direct effect on the environment.[17].

In recent years, the impact of the healthcare sector on the environment increased due to the covid crisis. According to Wuyts, the waste generation increased by 65% at the peak of the crisis [18]. The use of single-use technologies, already common in the pharmaceutical industry and deleterious for the environment, played an important role during the crisis because it helped to accelerate the vaccine production processes implementation [19].

4 Circular Economy & Pharmaceutical Industry: A review

In this part, the methodology followed to conduct the literature review is presented, then the classification of the papers studied is proposed to better understand how the existing literature is structured.

4.1 Methodology

To analyze the existing scientific literature on CE within the pharmaceutical industry, a semi-systematic literature review was performed [20]. Most of the research was done by using google scholar or science direct and numerous scientific papers and publications were analyzed. Specific keywords corresponding to the areas of CE and pharmaceutical industry/drug development were used. The articles corresponding to the criteria were selected.

4.2 Classification of the literature

As it was mentioned previously, the number of publications on the CE has been increasing through the years. The analysis of the literature on the CE within the healthcare sector has also proven the same tendency, this topic is on the rise and many stakeholders of this sector are willing to consider this new model in their practices.

The complexity of this research can be explained by the broadness of the scope regarding the CE field and its potential applications. In recent years, many papers including specific terms such as “circular economy” and “pharmaceutical industry” were published. In their study, Ang et al. identified 182 publications linked to circularity in the pharmaceutical industry [5]. As it is well explained in their article, each paper corresponds to CE principles from the 9R framework. An analysis of the cited publications allowed us to identify that in many papers, the terms “pharmaceutical industry, healthcare sector, medical industry” are not mentioned. The publications refer to CE principles and propose diverse ways to reach circularity, but they do not always focus on the pharmaceutical industry. Nevertheless, even though some articles do not specify the aforementioned keywords, those papers are still relevant because they propose circular actions for specific processes, waste treatment, etc., which could directly be implemented into the pharmaceutical industry processes. Therefore, many articles cannot be directly linked to the pharmaceutical sector because their purpose is to improve different manufacturing processes in general, for different types of industries. Yet, it is still understandable to categorize those papers into pharmaceutical circularity. This enlightens the complexity linked to the categorization of this literature. It is not an easy task to determine which publication concerns the pharmaceutical industry or not, due to the several development processes (chemicals, biologicals) and the number of circularity possibilities within this sector.

Moreover, the papers’ study permitted the identification of additional classification parameters: fundamental versus applied research, and scientific literature versus standards and regulations. On a higher level, the semi-systematic literature review conducted highlighted the fact that two types of papers stand out: papers focusing on strategy and

management, with action plans, public awareness improvement propositions, etc.; papers focusing on the operational level, with solutions for waste management, or solutions regarding alternative chemistry/ process/ functions.

This literature review allowed a better understanding of the existing literature on the CE in general, and to understand how it takes place in the pharmaceutical industry. This topic has gained interest in recent years, not only in the research field but also in many industries and for national /international authorities. The current trends emphasize the future growing evolution of this topic and the necessity for pharmaceutical stakeholders to implement this concept into their goals and practices.

5 Proposal of mapping for CE into the healthcare sector

5.1 Mapping

The previous parts of this paper emphasize the crucial role of the life cycle in the improvement of the environmental performance of products or services. Therefore, the classification of the papers analyzed throughout the literature review was done regarding the life cycle steps of a product. However, it was decided not to select the generic life cycle stages proposed by the eco-design approach. The diagram from Luu, adapted from Keoleian and Menerey, 1994 [21], was chosen for the realization of the mapping, it represents the life cycle stages selected to categorize each paper.

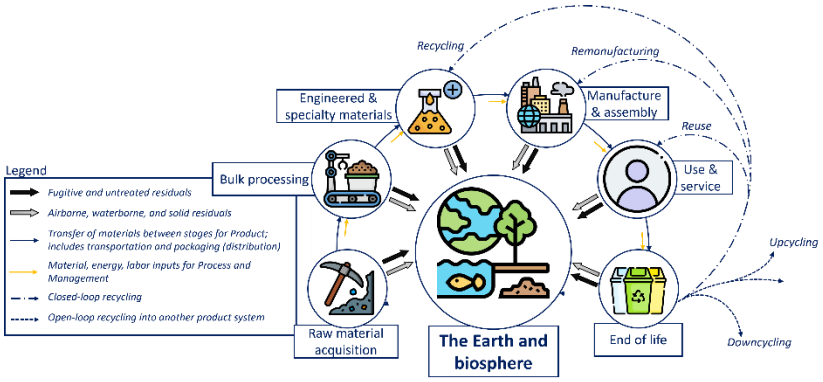

Fig. 1. Generic life cycle of a product integrating short, medium, and long CE loops

As we can see, six different steps compose this life cycle and all of them refer to the elementary level called “The earth and biosphere”. According to Keoleian and Menerey, this level helps us to understand that each product (and life cycle stage) requires resources from the earth and biosphere to be created and generates waste that accumulates in the same place. Surrounding this elementary level, we can find the main life cycle steps of a product. At first, there is the raw material extraction, then, the bulk processing and engineered & specialty materials, afterwards there is manufacturing & assembly, then, use & service, and finally the end of life. This diagram is interesting

because it allows the identification of numerous loops, and thus, the identification of different CE frameworks. As an example, the link between end-of-life and the earth and biosphere can be considered as the biological cycle from the EMF butterfly diagram.

The selection of those life cycle stages instead of others was based on several assumptions. The transport/distribution steps are represented by the arrows connecting the life cycle stages. This does not mean that no circular actions can be implemented regarding this specific stage, but more importantly that it can be considered as an underlying part of the other stages studied. The main differences with this diagram are the additional steps in between the raw material acquisition and the manufacturing & assembly. Those steps are respectively named bulk processing and engineered & specialty materials. The CE is based on different principles such as "Reduce, Reuse, Recycle" which require a focus on resources and materials [22]. Because they are the main drivers in CE, it was considered that adding more stages regarding these elements was essential. The literature review conducted, and analyses of the papers ended up with the categorization of each paper regarding the aforementioned life cycle steps. The following diagram depicts the number of times the topics are studied in the different papers.

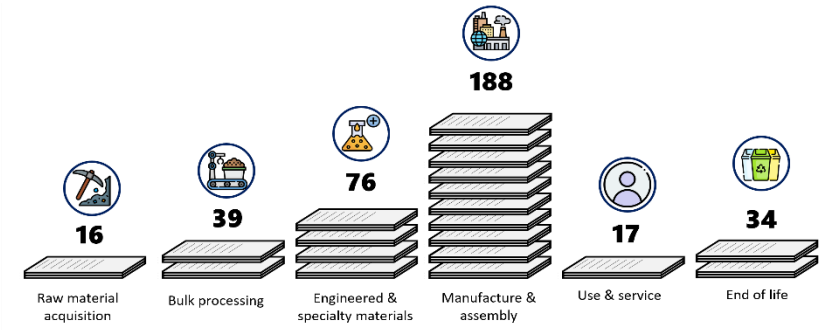

Fig. 2. Breakdown of CE-related topics in the pharmaceutical industry mentioned in the literature, regarding product life cycle steps

A little bit less than 300 publications were analyzed resulting in 370 topics mentioned. There are publications that focus on several topics. The 182 publications cited in the framework proposed by Ang et al., to implement the CE into the pharma industry were assessed, and more than one hundred additional articles published in the last four years, found on google scholar were selected. This chart depicts the current trends in terms of CE within the pharmaceutical industry. It is easily identifiable that most of the papers published focus on the manufacture & assembly step. The second part with the highest number of publications is "engineered & specialty materials", closely followed by the bulk processing part. Then, there is the end of life, with less than 40 papers, and finally, the raw material acquisition and the use & service parts, with fewer than 20 publications.

To achieve CE goals and principles, each life cycle step of the product/service has to be considered with the aim of reducing the corresponding environmental impacts. It is not new that every life cycle stage generates impacts that need to be tackled.

Nevertheless, the mapping proposed highlights some differences between the number of publications available for all the steps. Hence, we can question the significant difference in the number of publications available for each stage.

Results Interpretation.

There are only a few publications that address the issues of raw material acquisition and use & service. Due to its main principles, it can be understood that the raw material stage is not the first focus because it is more important to reuse or recycle resources already in the loops than to extract new ones from the earth. The European Commission is part of many of those papers, as an example, they published a chart for raw materials resilience. Papers with a larger scope, focusing on several life cycle steps including raw materials and use/service, were proposed in the last few years, such as the new packaging and plastic waste regulation proposal or the CE action plan. The European Federation of Pharmaceutical industries and Associations (EFPIA) released a white paper on CE in the pharmaceutical sector tackling several issues such as the use phase and public awareness. Despite this type of paper, only a very low number of scientific papers are available in the literature regarding the scope of our study.

Referring to the waste management part, the scarce number of articles available can be surprising, mostly when thousands of articles tackling the management of waste can be found in the literature. Nevertheless, this can be explained by the fact that only a few papers consider the waste resulting from the use phase of a product (e.g.: expired medicines brought back to the pharmacy by the patient). Papers considering the issue of waste management in the pharmaceutical industry mainly focus on manufacturing waste. In this study, it has been considered that this kind of waste management is part of the manufacturing process. This argument that explains the huge quantity of publications dealing with the manufacturing stage.

The articles' analysis did not permit a deep review of those papers, and thus can have limited our understanding. In consequence, the differentiation between papers classified in bulk processing or engineered materials cannot be completely accurate. Therefore, we considered that those parts can be gathered. Consequently, together they represent the second highest focus. In this category, many papers study the transformation of waste from other sectors to resources for the pharmaceutical industry (e.g.: the transformation of pig mucosa into low-molecular weight heparin).

Finally, the most consequent part, manufacture & assembly, has been the main focus for science during the last years. Numerous papers discuss new molecular entities or new synthesis processes to improve the yields and decrease the environmental burden of the drug development process. Regulatory constraints may also contribute to the large number of publications on this topic.

5.2 Limits & Opportunities

This mapping is interesting because it emphasizes the current trends in the pharmaceutical circularity field. What we can conclude from it is the significant number of opportunities linked to the implementation of CE in the pharmaceutical sector. It is possible to identify where the major issues for the healthcare sector are and where

further research should be conducted. As an example, the toxicity of the medicines on the environment is of high importance and the link between ecotoxicology and circularity needs to be further investigated, thus potentially increasing the number of publications for the end-of-life step. The growing use of biotechnologies for the development of drugs may also bring circular solutions regarding the raw materials acquisition. Those technologies based on biological systems and living organisms could represent opportunities for the production of drugs from renewable raw materials or intermediates, but the global environmental footprint should be considered.

The elements mentioned above can also reflect the limits of this paper. The mapping proposed can be considered as a preliminary mapping as the literature review conducted did not allow the analysis of all the existing literature on this topic. As it was presented, the keywords used for the research, or the chosen criteria, did not provide a complete view of the available papers. Nonetheless, this is the first approach to this topic and this preliminary review allows the identification of a trend in the examined publications. This literature review, depicted as preliminary, needs to be further investigated. The following elements are ideas that could help to conduct a deep and detailed literature review. First, it is important to add additional keywords in the research, such as “drug, medicine, medical, ecotoxicology, biotechnology, etc.”. Second, the analysis of each selected article has to be thorough. Here, for most of the articles, only the abstracts were read, thus limiting the ability to clearly identify specific details of each paper article. Finally, the trending topics identified can help to foster research in those fields of research.

6 Conclusion and future work

The CE is a recognized approach that helps to tackle the biggest environmental challenges from the 21st century, moving from a linear model to a circular one. The number of publications available on this topic is increasing each year making it one of the most trending topics when talking about environmental sustainability. Due to its processes and the nature of its products, the pharmaceutical industry has significant impacts on the environment. Therefore, it is crucial that the CE can be implemented in the pharmaceutical industry especially since circular principles are not fully embedded yet.

This paper defines a mapping of the publications available in the literature about the CE within the pharmaceutical industry. To reach this objective, we identified life cycle steps in accordance with the CE that could represent the stakes of circular actions. The analyzed publications were sorted into each life cycle stage of the product. The mapping proposed emphasized the high number of papers in two stages of the product life cycle. This classification not only allows the identification of potential solutions to implement the CE into the pharmaceutical industry but also permits the identification of opportunities for future research.

This study acknowledges the broadness of the scope of the CE when it comes to circular principles implementation. However, this preliminary review presents the basis for further study in the field of circularity for pharmaceutical industries and highlights a certain level of uncertainty with the needs for a deeper literature review.

References

1. Kirchherr, J., Reike, D., Hekkert, M.: Conceptualizing the circular economy: An analysis of 114 definitions. Resources, Conservation and Recycling 127, 221–232 (2017).
2. Ellen MacArthur Foundation. Towards the circular economy Vol. 1: an economic and business rationale for an accelerated transition (2013).
3. Panza, L., et al.: Open product development to support circular economy through a material lifecycle management. . Int. Jour. of Product Lifecycle Management 14(2/3), (2022).
4. Circle Economy.: The Circularity Gap Report 2023. Amsterdam (2023)
5. Ang, K. L., et al.: Sustainability Framework for Pharmaceutical Manufacturing (PM): A Review of Research Landscape and Implementation Barriers for Circular Economy Transition. Journal of Cleaner Production 280(2), 124264 (2020).
6. Ranjbari, M., et al.: Mapping healthcare waste management research: Past evolution, current challenges, and future perspectives towards a circular economy transition. Journal of Hazardous Materials 422, 126724 (2022).
7. UNEP.: 21 Issues for the 21st century: results of the UNEP foresight process on emerging environmental issues (2017).
8. Rockström et al.: Planetary Boundaries: Exploring the Safe Operating Space for Humanity, Ecology and Society 14, 3-32 (2009).
9. Bocken, N.M.P., et al.: Product design and business model strategies for a circular economy, J Industrial Prod Eng 33, 308–320 (2016).
10. EU.: A New CE Action Plan For a cleaner and more competitive Europe. (2020).
11. EC.: Proposal for a Regulation establishing a framework for setting ecodesign requirements for sustainable products and repealing Directive 2009/125/EC (2022).
12. McKinsey's Center for Business and the Environment, Ellen MacArthur Foundation: Growth within: a circular economy vision for a competitive Europe (2015).
13. Luu, D.-N., et al.: Eco-design and medicine: Opportunities to implement eco-design in the pharmaceutical R&D process. J Clean Prod 365, 132785 (2022
14. Eckelman, M.J. et al.: Health Care Pollution And Public Health Damage In The United States: An Update, Health Affair 39, 2071–2079 (2020).
15. Ogden, N. Gachon, P.: Climate change and infectious diseases: What can we expect? Can Commun Dis Rep 45, 76–80 (2019).
16. Wilkinson, J.L. et al.: Pharmaceutical pollution of the world's rivers, Proc National Acad Sci 119, e2113947119 (2022).
17. Pimentel, D. et al.: Ecology of Increasing Diseases: Population Growth and Environmental Degradation. Hum Ecol 35, 653–668 (2007).
18. Wuyts, W., et al.: Circular economy as a COVID-19 cure? Resources, Conservation & Recycling 162, 105016 (2020).
19. Luu, D.-N. et al.: Recycling of Post-Use Bioprocessing Plastic Containers - Mechanical Recycling Technical Feasibility, Sustainability (2022).
20. Snyder, H.: Literature review as a research methodology: An overview and guidelines. Journal of Business Research 104, 333–339 (2019).
21. Keoleian, G.A., Menerey, D.: Sustainable Development by Design: Review of Life Cycle Design and Related Approaches. Air Waste 44, 645–668 (1994).
22. Saidani, M.: Monitoring the circular economy with circularity indicators, Applications to the heavy vehicle industry, Ph.D. thesis, Paris-Saclay (2018).