Carbon Footprint of 3D-Printed Bone Tissue Engineering Scaffolds: An Life Cycle Assessment Study

Nurul Ainina Nadhirah Tajurahim, Salwa Mahmood, Muhamad Zameri Mat Saman, and Nor Hasrul Akhmal Ngadiman

***Abstract*—The bone tissue engineering scaffolds is one of the methods for repairing bone defects caused by various factors. According to modern tissue engineering technology, three-dimensional (3D) printing technology for bone tissue engineering provides a temporary basis for the creation of biological replacements. Through the generated 3D bone tissue engineering scaffolds from previous studies, the assessment to evaluate the environmental impact has shown less attention in research. Therefore, this paper is aimed to propose the Model of life cycle assessment (LCA) for 3D bone tissue engineering scaffolds of 3D gel-printing technology and presented the analysis technique of LCA from cradle-to-gate for assessing the environmental impacts of carbon footprint. Acrylamide (C_3H_5NO), citric acid ($C_6H_8O_7$), N,N-Dimethylaminopropyl acrylamide ($C_8H_{16}N_2O$), deionized water (H_2O), and 2-Hydroxyethyl acrylate ($C_5H_8O_3$) was selected as the material resources. Meanwhile, the 3D gel-printing technology was used as the manufacturing processes in the system boundary. The analysis is based on the LCA Model through the application of GaBi software. The environmental impact was assessed in the 3D gel-printing technology and it was obtained that the system shows the environmental impact of global warming potential (GWP). All of the emissions contributed to GWP have been identified such as emissions to air, freshwater, seawater, and industrial soil. The aggregation of GWP result in the stage of manufacturing process for input and output data contributed 47.6% and 32.5% respectively. Hence, the data analysis of the results is expected to use for improving the performance at the material and manufacturing process of the product life cycle.**

***Index Terms*—Life cycle assessment, environmental impact, global warming potential.**

I. INTRODUCTION

Tissue engineering (TE) scaffold technology provides a temporary basis for the creation of biological replacements for the repair, maintenance, or enhancement of tissue function or a damaged organ. 3D bone tissue engineering uses 3D printing technology to support or repair damaged bone generated from various causes [1]. Besides, bone tissue engineering is a way of recovering bone defects generated from various causes. In general, there are three main elements for bone tissue construction and regeneration in vivo and in vitro, which are the combination of seed cells, growth factors, and scaffold materials [2]. In recent years, bone tissue engineering has become an important approach for repairing bone defects where scaffolds play an important role in ensuring the success of this type of bone engineering [3]. The preparation of materials is one of the important factors to be considered in developing 3D-printed bone tissue engineering scaffolds. The ideal bone scaffolds should be able to repair the bone defect and restore the bone tissue function [4]. 3D printing technology is preferred as a manufacturing process for the application of TE. As a result of its rapid fabrication, high precision, and customizable fabrication, 3D printing technology offers an advantage in the manufacture of a scaffold for TE applications which are fast, effective resolution, and can be produced in both basic and complex forms [5]–[8]. Furthermore, this technology can produce a successful result in the formation of complex, well-defined, and can be designed based on the 3D medical scan data of individual patients [8]. 3D printing technology also provided the compressive strength of human fibrous bone tissue [9]. Fig. 1 shows the concept of skeletal tissue regeneration via scaffold-based tissue engineering strategies.

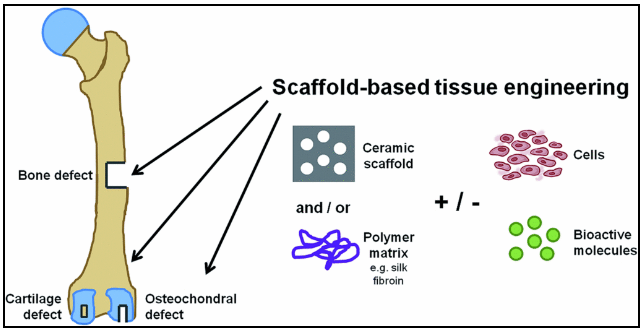

Fig. 1. The concept of skeletal tissue regeneration via scaffold-based tissue engineering strategies [10].

The preparation of materials is one of the important things on making a 3D bone tissue engineering scaffolds. The ideal bone scaffolds should be able to repair the bone defect and restore the bone tissue function [4]. Referring to the previous research, the material extraction that has been used is basically involved with the polymer, ceramic, composite and hydrogel. All those materials have their own properties to characterization [2], [10]-[17]. The choice of materials for tissue engineering makes up a significant portion of influence on the performance of scaffolds [18]. Besides, the 3D printing technology is preferred as a manufactured process

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for the application of TE. These methods can produce a result in the formation of complex, well-defined and can use via computer-aided design (CAD) Model and computer controlled of computer-aided manufacturing (CAM) tool handling.

In most cases, values processes in 3D printing technology were portrayed as advantageous in terms of reported global warming potential (GWP). The majority of papers detailed result ranges that indicated various printing, manufacturing, or distribution tactics in which 3D printing performance varied significantly [19]. Therefore, LCA was important in determining the best production method, and it appears to be a useful lens for ensuring 3D printing's environmental performance. According to some evaluation, there is a change in the contribution of materials and manufacturing methods in the life cycle GWP loads of systems manufactured with 3D printing technology and conventional manufacturing. 3D printing technology contributed to about 80% of the total GWP, whereas conventional manufacturing was maintained in the position by material-related loads [19].

LCA is indeed a valuable tool for conducting a complete environmental impact assessment of 3D bone tissue engineering scaffold and an important tool for assessing the environmental impact from different types of system boundaries. The development of 3D bone scaffolds involves the stage of material selection and manufacturing processes that also consume a high amount of energy. Generally, the environmental impact is caused by the manufacturing process. The environmental exposures contribute towards energy consumption and pollution emission to land, water, and air.

In addition, LCA is a technique or tool to evaluate the potential environmental impacts associated with all the stages of the product’s life ranging from raw material extraction through material processing, manufacture, distribution, usage, maintenance, and disposal or recycling [20]. The purpose of LCA is to understand the flow of matter and energy involved which can be assigned to products and services by quantifying all inputs and outputs of material flow. Besides, it can also be utilized to examine the environmental critical points so that preventive measures can be taken [21]. According to the ISO 14040:2006, LCA is a tool for assessing the potential environmental aspects and potential aspects associated with a product or service. It is done by compiling an inventory of inputs and outputs, evaluating the potential environmental impacts with those of inputs and outputs, and interpreting the results concerning the objectives of the study [22]. Besides, there are variants of LCA that can be used for the LCA study, which are cradle-to-grave, cradle-to-gate, cradle-to-cradle, or closed-loop production, gate-to-gate, well-to-wheel, economic input-output LCA, ecologically-based LCA, and exergy based LCA [23]. Table I tabulates the four kinds of main different variants that are commonly used in the LCA study.

According to ISO14040:2006, the first prerequisite of LCA methodology is the selection of system boundaries. The system boundary can indeed be interpreted as the phases or stages of the production process to be integrated into the framework. The selection of system boundary analysis depends on the analyses' purpose, interpretation, and scope. The results of the assessment may slightly differ when considering the different system boundaries [25]. Life cycle stages, unit processes, and flows, such as raw materials, inputs during processes, energy consumed, and other related life cycle phases, should be considered in setting the system boundary. Fig. 2 shows the schematic flow of the system boundaries of LCA with the cradle-to-grave, cradle-to-gate, and gate-to-gate data sets as parts of the complete life cycle.

TABLE I: THE DIFFERENT VARIANTS OF LCA

No.	Types	Descriptions
1	Cradle-to-grave	The full LCA from resource extraction (cradle) to the usage and disposal stage (grave).
2	Cradle-to-gate	An assessment of partial product life cycle from resource extraction (cradle) to the factory gate [24].
3	Cradle-to-cradle or closed-loop production	The concept is often referred to within the circular economy. It is the specific assessment of cradle-to-grave by exchanging the waste stage with a recycling process that makes it reusable for another product (closing the loop).
4	Gate-to-gate	A partial LCA looking at only one value-added process in the production chain is assessed.

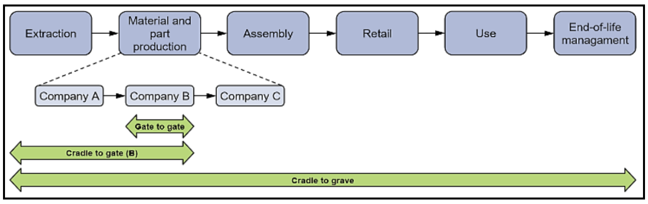

Fig. 2. The concept of skeletal tissue regeneration via scaffold System Boundaries of LCA [26].

This paper seeks to propose an LCA Model to assess the environmental impacts namely, the depletion of natural resources, energy consumption, and emission to land, water, and air. The research is also aimed at identifying the environmental impacts of 3D Bone Tissue Engineering scaffolds from cradle-to-gate. Besides, the use of LCA enables the identification of various opportunities to improve the environmental performance of the product at various points in the proposed tissue engineering scaffold life cycle by using the GaBi Software. Besides, the LCA from cradle-to-gate of system boundary analysis technique is also used in this study to assess the environmental impacts from selected materials and manufacturing processes.

To assess the environmental impacts, the study of LCA is indispensable, which is LCA Model capable of evaluating the possible environmental effects associated with all phases of the life cycle of a product. In addition, LCA helps educate industry, government, or non-governmental decision-makers about strategic planning, goal setting, process design, or redesign based on impacts on the environment. The outcomes of this research was identified the weak areas related to environmental aspects. Furthermore, the TE scaffold can be improved to reduce the environmental burden.

The LCA Model is used to identify the environmental impacts of 3D Bone Tissue Engineering scaffolds by using GaBi software. The development of LCA Model will provide the specification of input and output parameters for materials, manufacturing processes, and energy consumption. Thus, it is believed that the development of LCA Model is very helpful to graphically assess the potential environmental impact associated with the material and manufacturing processes of a product's life cycle. The intended to assess the environmental impact is to make the production process more environmentally friendly.

II. PROPOSED LCA MODEL

The development of LCA Model was conducted according to the ISO 14040 standards. The sequence of the Model followed the methodological framework of LCA governed by the international standard ISO 14040, which defined four main phases for the study of LCA. LCA Model in this research is the life cycle of the 3D-printed bone tissue engineering scaffolds, referring to the major activities in the course of the product's life-span from the material required to manufacture the product. The system boundaries in the LCA Model development of 3D-printed bone tissue engineering scaffolds in this research consist of two stages that begin with the selection of materials and the manufacturing processes used. Thus, consideration was given to all phases of LCA approach set out in the regulatory framework. The analytical findings are presented through graphs generated by GaBi software based on the inventory of each material and manufacturing process used. In this research, the technology of 3D printing manufacturing uses 3D gel-printing which is the indirect inkjet printing (DIP) technology. It can be seen that some previous studies had successfully prepared 3D printing manufacturing using DIP technology [27]. Besides, the selected manufacturing process in this research is using the material of porous Hydroxyapatite (HA) scaffolds which are selected based on the previous study [27].

A. Data Collection

TABLE II: DESCRIPTIONS OF DATA

Life cycle stage	Type of data	Description	References
Material selection	Primary data	HA slurry which are the rheological properties of the HA ceramic slurry	(Shao *et al.*, 2019)
	Secondary data	The emission factor of the composition of material and components.	(Yung *et al.*, 2018)
Manufacturing process	Primary data	3D gel-printing technology	(Shao *et al.*, 2019)
	Secondary data	Emission factors of energy which electricity.	(Yung *et al.*, 2018)

The data of the unit process obtained for the material selection and manufacturing process were primarily collected according to previous research works. The selected material and manufacturing process chosen are HA slurry and 3D gel-printing technology respectively [27]. Besides, the secondary data in which the emission factor used were as local as possible with considerations related to geography, technology, and time [28]. Table II shows the details of the data used in this research. References to the GaBi database are used if the parameter from the previous research is not available. The unavailable data will directly be changed with similar materials or processes using the GaBi database. The GaBi database provides information on the environmental burdens and benefits in terms of their production. The information yielded is described as the consumption and the saving of resources energy that releases or reduces emission to air, water, or soil [29].

B. Parameter Involved

The elementary input and output flow of the 3D gel-printing technology are described using the LCA Model developed. The fundamental input and output flow that crosses the boundary of the system is used as input parameters to determine the selected phases. The input flows such as chemical reagents and raw material powder are required to produce the 3D printed Model. The output flows include the emissions produced from the system boundary. The elementary input and output flow of the 3D gel printing technology crossing the system boundary is presented in Fig. 3.

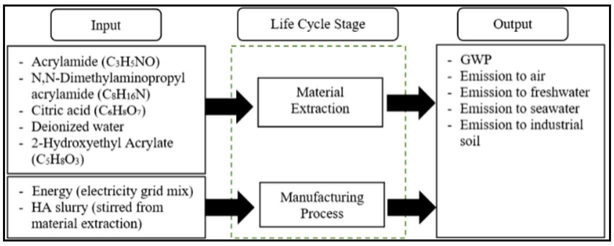

Fig. 3. Elementary input and output flow crossing the system boundary of 3D gel-printing technology.

C. Material Phases

The material selected for the 3D gel-printing technology depends on the slurry preparation and material extraction that include their characterization. The preparation of material is organized into three stages which are the premixed solution, the addition of the raw material powder, and the mixing process. The typical chemicals used for 3D gel-printing technology with their specific category is shown in Table III, while, Table IV tabulates the description of the material used with its weight distribution. These materials are categorized according to the GaBi database [29].

TABLE III: MATERIALS USED FOR 3D GEL-PRINTING TECHNOLOGY WITH SPECIFIC RESOURCES

No.	Category	Chemical/material used	Resources
1	Chemical reagent	C_3H_5NO	Organic intermediate product
2	Cross-linking agent	$C_8H_{16}N_2O$	Non-methane volatile organic compounds (NMVOCs)
3	Dispersant	$C_6H_8O_7$	Organic intermediate product
4	Solubilization	H_2O	Renewable resources
5	Raw material powder	$C_5H_8O_3$	Non-methane volatile organic compounds (NMVOCs)

D. Sample Calculations

The sample calculation is drawn to obtain detailed values of the flow for the material phase as follows:

- In order to produce 1 kg of premixed solution = 0.00001226 m^3
- In order to produce 1 kg of HA slurry = 0.00002726 m^3

TABLE IV: DESCRIPTION OF THE MATERIALS USED WITH THEIR WEIGHT DISTRIBUTION

No	Chemical/material used	Weight (kg)	Weight Distribution (%)
1	C_3H_5NO	0.0012	4.40
2	$C_8H_{16}N_2O$	0.00016	0.59
3	$C_6H_8O_7$	0.0009	3.30
4	H_2O	0.01	36.68
5	$C_5H_8O_3$	0.0015	55.03
	Total	0.02726	100

E. Manufacturing Process

3D gel-printing technology is selected as the manufacturing process in which the process was prepared by using selected materials. In this study, the specific process of printing the HA scaffolds or 3D Model is tabulated in Table V. The specific 3D gel-printing process consumes energy which is the electricity of electric power.

TABLE V: SPECIFICATION OF MANUFACTURING PHASES

No	Category	Process used	Flow Quantities
1	Auxiliary processes	3D gel-printing technology	1 kg
2	Energy	Electricity grid mix	0.0001 MJ

F. Application of LCA Phases

To conduct the inventory analysis, the data of the materials and processes used which include energy consumption and chemical substances were collected. The data and processes involved are analyzed to assess the environmental impact based on the environmental assessment. The impact assessment is to provide additional information which is to help assess the life cycle inventory (LCI) performance of a production process. Therefore, the strategic arrangement is used to propose an LCA Model for 3D bone tissue engineering scaffolds. In this research, the application of ISO 14040:2006 steps are as follows:

- Goal and scope definition; this research seeks to propose an LCA Model of 3D bone tissue engineering by applying the selected manufacturing process which is 3D gel-printing technology. The LCA approach is utilized to assess the environmental aspects and potential impacts of 3D bone tissue engineering scaffolds. The LCA Model in this paper is referring to the major activities in the course of the product's life-span from the material required to manufacture the product which the stage of the manufacturing process. The system boundaries in the LCA Model development of 3D bone tissue engineering scaffolds in this paper consists of two stages. These stages begin with the selections of materials and the manufacturing processes used. Thus, the consideration was given to all phases of the LCA approach set out in the regulatory framework. The analytical findings are presented through graphs generated by GaBi software based on the inventory of each material and manufacturing process used. According to the determination of the system boundary in this paper, the cradle-to-gate stages will be covered for the system of the product life cycle stages. The system boundaries of 3D bone tissue engineering scaffolds define which unit processes based on the 3D-printed scaffolds. This system consists of two kinds of production stages which begin with the selections of materials and the manufacturing processes used. Hence, all the unit processes included in this paper contributed directly from cradle-to-gate life cycle stages to the end of results.
- Inventory analysis; the LCI is used to balance the mass and energy, and also to qualify all materials and emissions through the system boundaries. The energy consumption used in the manufacturing process and the materials input for the system are identified. GaBi software was used to utilize emissions and other environmental impacts.
- Impact assessment; the significance of potential impacts on the environment is assessed using the LCI results. LCA flow begins with the selection of the parameter category and the characterization of the Model. Other specific elementary is also applied to the system, such as the weighting and other grouping categories. Categories of environmental impacts are quantified from the whole 3D bone tissue engineering scaffolds system, such as GWP and emissions.
- Interpretation; according to the results obtained in the impact assessment, the potential environmental impacts according to the development of an LCA Model for 3D bone tissue engineering scaffolds were evaluated and discussed.

III. RESULTS AND DISCUSSION

A. Development of Proposed LCA Model

LCA Model for the development of 3D gel-printing technology focused on the selected materials and manufacturing processes, which were referred to as Model quantities. The materials are commonly categorized as either renewable or non-renewable resources and have also been classified as an intermediate organic or inorganic component. The potential negative environmental impact involving the non-renewable resource is the H_2O as a solubilization agent. The material phase is separated into two stages namely slurry preparation and material extraction. Firstly, the slurry was prepared using the chemicals which were 0.0012 kg of C_3H_5NO, 0.00016 kg of $C_8H_{16}N_2O$, 0.0009 kg of $C_6H_8O_7$. These chemicals were then dissolved into 0.01 kg of H_2O. Next, the material extraction is prepared by adding the HA powder which is 0.015 kg of $C_5H_8O_3$ to the prepared premixed solution which produces raw material powder known as HA slurry. Besides, the materials are selected based on the findings from previous studies, and some of the materials were changed according to the availability on the GaBi database. After the material extraction was completely done, the prepared slurry is loaded into the manufacturing process to produce the 3D Model for bone tissue engineering scaffolds. In this study, the specific 3D gel-printing process consumes energy. Fig. 4 illustrates the schematic diagram of the LCA Model for 3D gel-printing technology.

The advantage of establishing an LCA Model for 3D gel-printed bone tissue engineering scaffolds is to specifically determine the parameters for the materials and processes input and output. The parameter identification in 3D gel-printing technology refers to the phases of the developed system boundary. The parameter involved is obtained from the GaBi software database, and the potential environmental impact was generated through the development of the system boundary.

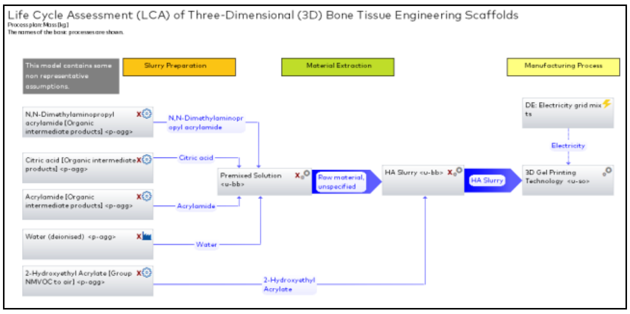

Fig. 4. The schematic diagram of LCA Model for 3D gel-printing technology.

B. Global Warming Potential

In the GaBi software, the characterization factor is applied to the obtained results. Characterization identifies and validates the impact of the evaluated 3D gel-printing technology system on the environment. Therefore, all of the emissions contributing to GWP had been identified. The quantity of flows that contribute to GWP originates from electricity consumption, manufacturing process, and material resources such as the premixed solution which act as chemical reagents and HA slurry which is a mixed slurry of selected chemicals and raw material powder used.

The results of GWP is represented in two sections which are the aggregation of input and output data. The data is shown in the unit of the kilogram (kg) for material resources and mega joule (MJ) for electricity. The GWP for input data involved the contribution of emission to air which resulted from 1 kg of 3D gel-printing technology, 0.015 kg of $C_5H_8O_3$, and 0.015 kg of HA slurry. According to the graph, the other data graphically shows the input resources which are the energy and material resources. The material resources are 1 kg of HA slurry, 0.01 kg of H_2O, and 0.01 kg of the premixed solution, while energy resource is obtained from 0.0459 kg of electricity consumption. Whereas other resources which contributed a small amount resulted from the valuable substances which are 0.0012 kg of C_3H_5NO, 0.0009 kg of citric acid, 0.00016 kg of $C_8H_{16}N_2O$, and 0.00226 kg of premixed solution. Fig. 5 shows the bar graph of aggregation for input results that contributed to GWP.

According to the aggregation of output results, the quantity of flows that contributes to GWP involved the emission to air, emission to freshwater, emission to seawater, and emission to industrial soil. The contribution of emission to air is a result from 0.000422 kg of electricity consumption, 0.015 kg of $C_5H_8O_3$, and 1 kg of HA slurry. The emission to freshwater is yielded from 0.0468 kg of electricity consumption. Whereas, other emissions such as emission to seawater and emission to industrial soil originated from a small amount of energy consumptions which are 4.37×10-5 kg and 9.85×10-11 kg respectively. Besides, the valuable substances contributed were a result of the manufacturing phase and 1 kg of 3D gel-printing. For material resources, 0.0012 kg of C_3H_5NO, 0.0009 kg of $C_6H_8O_7$, and 0.00016 kg of $C_8H_{16}N_2O$ were involved in valuable substances. Furthermore, other data graphically show the contribution of output material resources which resulted from 1 kg of premixed solution and 0.01 kg of H_2O. Lastly, the small amount of deposited goods which is 9.97×10-5 kg is yielded from energy consumption. Fig. 6 shows the bar graph of aggregation for output results that contributed to GWP.

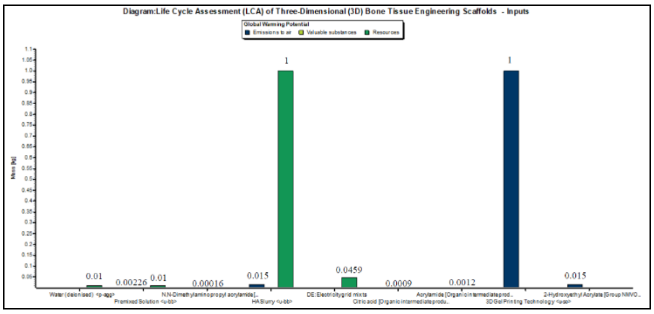

Fig. 5. Aggregation for input results that contributed to GWP of 3D gel-printing technology.

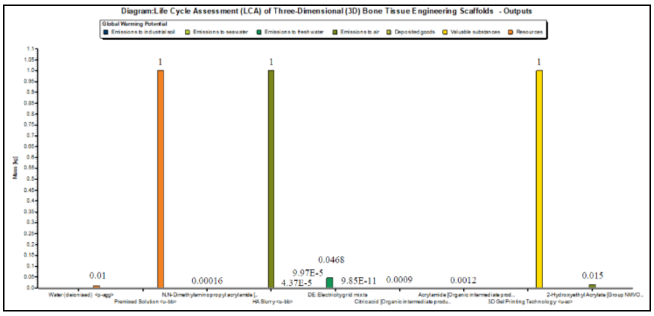

Fig. 6. Aggregation for output results that contributed to GWP of 3D gel-printing technology.

IV. CONCLUSION AND RECOMMENDATIONS

The parameters that are involved in the system boundary need to be identified at the earliest stage to develop the LCA Model. In this study, the most suitable parameters involved which are the selected materials and manufacturing phases were selected according to the previous studies. Hence, LCA Model was successfully developed by using the preparation of premixed solutions with the chemical reagents and HA slurry for material resources, while the 3D gel printing technology has opted for the manufacturing phases. Moreover, the parameters involved are obtained from the GaBi software database, and the potential environmental impact was generated through the development of the system boundary. According to the analysis that had been done, the environmental impacts of 3D gel-printing technology contributing to GWP originated from electricity consumption, manufacturing process, and material resources. The environmental hotspot of material resources or processes was determined according to the contributions to GWP. The issue of GWP is represented by the GWP impacts category. Any emissions to air, water, and soil that contribute to GWP are classified as contributors. Based on the results, it is shown that the quantity of flows that contributed to GWP involved the emissions to air, freshwater, seawater, and industrial soil.

Furthermore, the results also indicate that the impact category in the system resulted from the linking process of specific resources to the specific environmental issue. Hence, the data analysis of the results is expected to be used for improving the performance of the material and manufacturing process of the product life cycle. In addition, it can also be utilized to make the production process more environmentally friendly. The developed LCA Model for assessing the environmental impact can be further improved in future researches are the next researcher can be by extending the stages of system boundaries covering from cradle-to-grave depending on specifications characteristics of the entire life cycle. Also, further researches on the parameters involved in 3D bone tissue engineering scaffolds should be examined. Since the LCA study needs to perform with a large amount of data, the future researcher needs to make further research on the parameter involved in 3D bone tissue engineering scaffolds. It is to avoid any assumption parameter included in the development of the system boundary. The detailed parameter will lead to a solid conclusion of the research. The findings will be more reliable but the analysis complexity would increase.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

NAN Tajurahim and S Mahmood conducted the research and facilitated the resources; Tajurahim analyzed the data and wrote the paper; MZM Saman and NHA Ngadiman reviewed and verified the analyzed data. All authors had approved the final version.

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