Human health risk assessment framework for new water resource recovery-based bio-composite materials

Nativio, Arianna; Jovanovic, Oriana; Kapelan, Zoran; van der Hoek, Jan Peter

DOI
10.2166/wh.2024.168

Publication date
2024

Document Version
Final published version

Published in
Journal of Water and Health

Citation (APA)
Nativio, A., Jovanovic, O., Kapelan, Z., & van der Hoek, J. P. (2024). Human health risk assessment framework for new water resource recovery-based bio-composite materials. *Journal of Water and Health*, *22*(4), 652–672. https://doi.org/10.2166/wh.2024.168

Journal of Water & Health

IWA PUBLISHING

Journal of Water and Health Vol 22 No 4, 652 doi: 10.2166/wh.2024.168

Human health risk assessment framework for new water resource recovery-based bio-composite materials

Arianna Nativio [a,*], Oriana Jovanovic [a], Zoran Kapelan [IWA] [a] and Jan Peter van der Hoek [IWA] [a,b]

[a] Department of Water Management, Delft University of Technology, Stevinweg 1,2628 CN Delft, The Netherlands
[b] Waternet, Korte Ouderkerkerdijk 7,1096 AC Amsterdam, The Netherlands
*Corresponding author. E-mail: a.nativio@tudelft.nl

AN, 0000-0002-8359-3096; OJ, 0000-0003-1854-2329; ZK, 0000-0002-0934-4470; JPv, 0000-0002-0674-388X

ABSTRACT

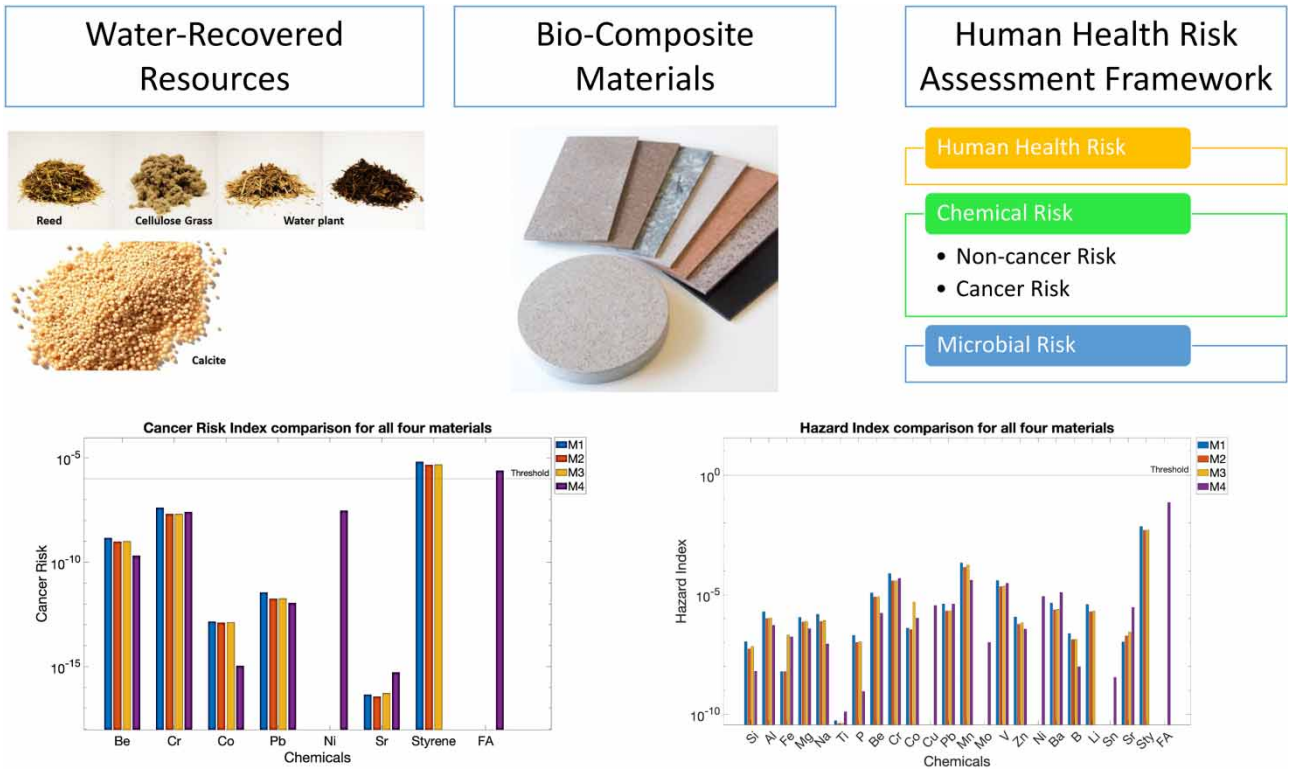
A new type of bio-composite material is being produced from water-recovered resources such as cellulose fibres from wastewater, calcite from the drinking water softening process, and grass and reed from waterboard sites. These raw materials may be contaminated with pathogens and chemicals such as *Escherichia coli*, heavy metals, and resin compounds. A novel risk assessment framework is proposed here, addressing human health risks during the production of new bio-composite materials. The developed framework consists of a combination of existing risk assessment methods and is based on three main steps: hazard identification, qualitative risk mapping, and quantitative risk assessment. The HAZOP and Event Tree Analysis methodologies were used for hazard identification and risk mapping stages. Then, human health risks were quantitatively assessed using quantitative chemical risk assessment, evaluating cancer and non-cancer risk, and quantitative microbial risk assessment. The deterministic and the stochastic approaches were performed for this purpose. The contamination of raw materials may pose human health concerns, resulting in cancer risk above the threshold. Microbial risk is also above the safety threshold. Additional analysis would be significant as future research to better assess the microbial risk in biocomposite production. The framework has been effectively used for chemical and microbial risk assessment.

Key words: bio-composite, chemical risk, human health risk, microbial risk, resource recovery, risk assessment

HIGHLIGHTS

- Production of new water resource recovery-based bio-composite materials.
- The safety of these materials, from production and application perspectives, needs to be assessed.
- Novel risk assessment framework focusing on human health risk assessment.
- Hazard identification, qualitative risk mapping, and quantitative risk assessment: QCRA and QMRA.
- Future research directions to improve the developed framework.

GRAPHICAL ABSTRACT



1. INTRODUCTION

Bio-composite materials are increasingly used in various applications, such as food packaging and the automotive industry. These materials are emerging as replacements for natural and conventional synthetic composites and plastic-derived materials. A trend is driven by the increasing awareness about green products by customers, government programmes, and new directives on waste management and recycling (Carvalho 2015). The most common biocomposites are made from natural fibres obtained from natural resources (e.g., cellulose), and their mechanical properties are comparable to those composites made from synthetic fibres (Roy *et al.* 2014).

Water and wastewater are considered valuable resources as they contain organic and inorganic substances that can be used for energy production and nutrient recovery (van der Hoek *et al.* 2016). In addition, the water smartness and sustainability of the technical solutions for reuse and resource recovery align with the United Nations' sustainable development goals n. 6 and n. 12 (SGD) (United Nations 2023).

A new type of bio-based material defined as *water resource recovery-based bio-composite* is emerging on the market and starting to be produced in the Netherlands. These novel bio-composite materials are largely made from renewable resources and, at the end of their life, can be ground and reused as a filler (up to 50% of the blend) in new biocomposites. According to data provided by the producers, these new materials are expected to remain durable for at least 30 years in aquatic environments. The use of natural fibres recovered, for example, from cellulose from wastewater requires significantly less energy to produce and fewer chemicals to adhere to the binder.

These novel materials are made from resources recovered from the water cycle, such as cellulose fibres from wastewater treatment plants (Ruiken *et al.* 2013), calcite pellets from drinking water treatment plants (Schetters *et al.* 2015), and materials from surface water management, such as aquatic plants. Once processed, these are bonded together using some polyester or bio-based resin to form a bio-composite material that can be used as a replacement for hardwood or other materials.

The production of bio-composite materials based on water resource recovery poses potential risks to human health. Several previous studies (Deng *et al.* 2018; Partyka & Bond 2022; Selvam *et al.* 2022) on surface water and wastewater reuse have clearly demonstrated the existence of these risks, with the main hazards arising from chemical and microbial contamination of various components. Zhang & Weng (2021) conducted a study on the potential hazards and associated risks in the production of plant fibre-derived bio-composite food packaging. The results indicated the potential for harmful substances, including melamine, to migrate from the packaging into the food, thereby posing a risk to human health. The presence of these substances can be attributed to the varying composition of plants, influenced by their respective environments. It is essential to consider these findings when evaluating the safety and viability of bio-composite food packaging. Therefore, certain harmful compounds, such as poisons like cyanide and melamine, are obtained from the plant. Other hazardous substances may derive from the use of additives and synthetic resins (e.g., monomers or polymers) to produce the bio-composites. Therefore, bio-composite materials based on water resource recovery should be assessed for their impact on human health risks during their production and use.

The present study aims to identify potential hazards and associated risks to human health that may arise during the production of a bio-composite material. The production process of bio-composite material typically involves the following steps (Mohanty *et al.* 2002): (i) raw materials preparation: the natural fibres, some of which may contain pathogens and chemicals, are cleaned, dried, and sometimes treated or disinfected to remove impurities or contaminants; (ii) matrix material preparation: the matrix material is dissolved in a solvent to create a liquid form: (iii) mixing: during this stage, the raw materials are blended with the liquid matrix component, resulting in the formation of dust that comprises pathogens and chemicals such as heavy metals. This dust can be ingested or inhaled by a worker or transferred by skin contact, posing a health risk; (iv) moulding: the mixture is poured or pressed to create the desired shape (e.g., plates); (v) curing: the mixture is left to harden and solidify; this process may require the material to be heated or cooled; (vi) finishing: the finished product may be sanded, painted, or coated to improve its appearance or functionality. The first four steps described earlier are the subject of this paper. Curing and finishing steps are not included, as these are highly dependent on the application of the bio-composite material.

During the moulding process, the mixed dough is pressed by a pressing machine (140–160 °C) for 1–2 min per mm of material thickness. This is a total of 4–8 min considering the thickness of the different bio-composite materials. It is expected that heat transfer would inactivate the remaining pathogens in the dough. However, the actual inactivation rate was not determined due to the lack of initial pathogen contamination data in the raw materials. In addition, no pre-treatment to reduce the heavy metal concentration has been carried out. The manufacturer can choose the quality of the raw material (e.g., utilize water board grass fibres instead of motorway grass fibres, which contain heavy metals and are unsuitable for use).

No concerns regarding exposure to drinking water, wastewater, or surface water are addressed in this study, nor are other risks such as environmental or material quality-related ones. Nevertheless, it should be pointed out that the final drinking water, treated wastewater, and surface waters, from which raw materials are obtained, meet legal and environmental requirements/standards. This paper examines the potential threats to human health from exposure to hazardous substances derived from raw materials or from the use of resins (e.g., monomers and polymers).

A risk assessment framework is needed to assess the health risks associated with the production of water resource-derived bio-composite materials. A previous study (Nativio *et al.* 2022) concluded that such a framework does not currently exist for these new materials and that the existing frameworks cannot be applied directly due to different means of human exposure and risk scenarios. For example, in the study conducted by Zubair *et al.* (2021), the authors concluded the necessity of standard operating procedure and hazard and operability study (risk assessment) to identify possible hazards associated with the production of biocomposites and minimize the risks during production. In another study, Singh & Lee (2015) evaluated the necessity of risk assessment due to the heavy metals contamination in automobile shredder residue (ASR) that is considered a dangerous waste in Europe. Based on the above, the purpose of this study is to develop such a risk assessment framework, i.e., a framework that can be used to assess the human health risks associated with the production of water resource recovery-based bio-composite materials.

The paper is structured as follows. Section 2 describes the materials and methods for producing these new bio-composite materials. Then, the new human health risk assessment framework is presented together with the associated methods used. Section 3 presents the results obtained when applying the new framework to the new materials, including a discussion of the

obtained results. Section 4 details the study's conclusions, outlining the functionality of the developed framework, the results obtained on human health risks, and the need for further research.

2. MATERIALS AND METHODS

In this section, a description of how the new materials are produced is provided in Section 2.1. Then, the developed framework is described step by step in the following sections.

2.1. New bio-composite materials

This work assesses the human health-related risks for four bio-composite materials (M1, M2, M3, M4) shown in Table 1.

These materials are produced using the following manufacturing steps:

1. The bio-composite production begins with the preparation of the dough. The resin (fluid) is added to the filler (e.g., calcite) and mixed for 20 min. The fibres are then added in the batches and mixed for 2–4 min. The fibres are added last and mixed for a shorter time to avoid breaking them. The mixing process allows the cohesion of all the raw materials, ensuring compatibility and adhesion. The mixing of raw materials can produce dust which may contain contaminants such as pathogens and heavy metals. In addition, the resin used in the production process can be toxic to human health due to the presence of hazardous substances such as styrene and furfuryl alcohol. These two substances are classified as hazardous to human health for both non-cancer and cancer risk. In addition, the use of the mixer requires training and the application of safety protocols (e.g., ventilated laboratory room). Therefore, personal protective equipment (PPE) such as organic vapour filtering respirators and butyl rubber or neoprene gloves (IFC 2022), depending on the exposure time, must be used to reduce exposure when handling raw materials, especially resins.
2. The dough obtained is then vacuum sealed in bags and left to mature in the refrigerator for a few days before being pressed. For M4, heating was used during the mixing process to decrease the water content. The additional step was not applied to materials made from polyester resin (M1, M2 and M3).
3. Finally, a moulding process is applied to give the product shape (e.g., panels). The materials are placed under the press (for the bulk moulding process). The dough is weighed and fed in, then the material is pressed for the time required to cure before the part is removed from the mould. At this stage, the safety protocols and training of the workers are required for the use of this type of machine. The use of this machine involves a risk of crushing, abrasions, cuts, and burns between man and machine. Therefore, the use of PPE is also required in this case.
4. The resulting moulds can then be machined according to the specific application of the material. This stage is not covered in this study.

This list shows that the main potential hazards are the presence of materials classified as hazardous to human health and the use of operating machinery that can lead to risks to human health. Specifically, in the production process of bio-composite, major concerns are the potential pollution due to the presence of pathogens, and chemicals such as heavy metals and resin constituents. Evaluation of operational machinery typically follows safety protocols provided by suppliers and personnel are trained on correct usage. Thus, this topic does not fall under the scope of this paper. Additionally, using appropriate PPE can reduce exposure and alleviate related effects.

This paper considers the handling of raw materials and resins without the use of PPE. The aim is to define the level of risk in the bio-composite production process by considering the worst-case scenario in terms of human health effects.

Table 1 | Composition of bio-composite alternatives

Type of material	M1	M2	M3	M4
Natural fibres	Water reeds	Water reeds	Wastewater cellulose	Grass
Filler	Mined calcite	Mix of drinking water calcite (from softening) and mined calcite	Mix of drinking water calcite (from softening) and mined calcite	Bio-filler from agricultural waste
Resin	Polyester resin	Unsaturated polyester resin with 50% bio-content	Unsaturated polyester resin with 50% bio-content	Furan resin
Additive	Confidential[a]	Confidential	Confidential	Confidential

[a]Additives are ingredients in a recipe that are considered confidential information from producers. However, the suppliers have confirmed that these additives do not significantly affect the overall evaluated risks.

2.2. Health risk assessment framework

This study uses the human health risk assessment framework to evaluate the potential risks associated with the production of biocomposites based on water resource recovery. The framework makes use of several existing methodologies that have been adapted and integrated together for this purpose. The framework is based on two main steps: (i) health risk mapping and (ii) quantitative risk assessment.

2.2.1. Health risk mapping: hazard identification and qualitative risk mapping

Risk assessment starts with hazard identification. Several methods have been used to identify hazards in the water sector, but not all of them seem to be directly applicable to hazard identification for the recovery of raw materials for the production of biocomposites (Nativio *et al.* 2022).

After an evaluation of different methods for hazard identification, such as failure mode, effects and criticality analysis (FMEA and FMECA) and What If Analysis, it was decided to use the Hazard & Operability (HAZOP) method here. The HAZOP method was originally developed to analyse chemical process systems in the early stages of process design in a chemical treatment plant, but it has since been extended to other types of systems (Haugen & Rausand 2011). The generic nature of the HAZOP method, combined with the ability to identify hazards using a structured, well-established methodology, makes it a preferred method for identifying hazards associated with the production of bio-composite materials based on water resource recovery. The HAZOP method is usually applied in the design phase, due to the novelty of the subject. Thus, the key hazards and associated risks are not really known due to the novelty of the topic.

The HAZOP analyses are usually performed by building a spreadsheet where the deviation is identified by combining guide words (e.g., *as well as* – an additional event occurs) with a process parameter (e.g., *influent water*). The combination of the guide words with the process parameters leads to additional events (in the example above, '*as well as influent water*'). This means that an additional event can occur such as the influent water not being disinfected, so the hazard is the potential growth of microbial biofilm that will have consequences. Once the deviation has been identified, the causes, effects, and safety measures are defined. Considering the production process of bio-composite, biofilm may be present on raw materials such as calcite pellets recovered from drinking water. The presence of biofilm implies the presence of microorganisms and can lead to contamination of the pellets and, consequently, the contamination of the bio-composite material causing a risk to human health.

The HAZOP method for bio-composite production was conducted; the scope was the identification of the hazards (deviations) and the potential effects based on a qualitative assessment. In this paper, the main deviations that may lead to risks to human health are selected. The aim is to identify the main potential hazards from the beginning of the process: preparation of raw materials used as fibres and/or filler to produce the bio-composite. The importance of this step is to define where the hazard that can cause a risk is present, and if necessary, where the safety guards or other safety barriers should be placed.

Once the hazards have been identified, they need to be linked to associated human health risks. This requires mapping the hazards to risks by identifying relevant intermediate cause and effect type events. The obtained result is a risk map that can be used to quantify the risks in the next stage of the assessment.

There are several methods for doing the mapping, including the failure mode effects and criticality analysis (FMECA), fault tree analysis (FTA), risk matrix and event tree analysis (ETA). FTA focuses on cause identification, which is not the object of this hazard mapping step in the risk assessment framework. Furthermore, both FMECA and risk matrix are semi-quantitative risk assessment methodologies. The output of these methods is a semi-qualitative characterization of the risk by assigning numbers describing the probability of occurrence and the severity of the risk. However, a semi-quantitative risk characterization is not the main objective of health risk mapping at this stage of the framework; rather, a methodology is required that produces a map of all potential risks associated with the bio-composite production process. To obtain such a map, an inductive methodology is required. This method must be able to define the impact of an identified deviation from the associated potential risks.

Based on the above, ETA was selected as the method for mapping the hazards to risks to produce bio-composite material based on water resource recovery. ETA is an inductive methodology that enables the definition of intermediate events that can lead to a scenario, which may or may not involve a risk, starting from an initial hazardous event. Usually, the standard ETA consists of a logical chain of events from the first hazardous event to the outcome. Furthermore, knowing the frequency of the first dangerous occurrence, it is possible to calculate the probability of each possible outcome (Center for Chemical Process Safety 1999).

In this framework, the ETA methodology is only applied qualitatively. To develop the qualitative ETA, only the branches that can lead to a potential risk scenario are considered. The common ETA scheme has an initial hazardous event, and a series of intermediate events, and safety barriers. In this qualitative ETA framework, the potential causes replace safety barriers and lead to the final scenario, which represents the risk. The identification of potential risks determines the appropriate measures needed to manage them.

The qualitative ETA scheme provides an overview of the hazardous events, the induced consequences, and the potential causes. Furthermore, a risk map can be created by collecting all the potential risks. The risk map shows which risks need to be assessed quantitatively based on the occurrence of the same risk category (e.g., chemical contamination).

The outcome of the hazard and qualitative risk analyses is a risk map shown in Figure 1.

As shown in Figure 1, the human health risks are related to chemical and microbial contamination of the raw materials. The main risks associated with the presence of microorganisms and chemicals, hazardous to human health, are assessed both qualitatively and quantitatively.

The health risk mapping mainly addresses raw materials collected from the water sector, such as cellulose from wastewater treatment, calcite pellets from drinking water treatment, and reed and grass from surface water management. Mined calcite, bio-filler, and resins at this stage were only considered based on safety data sheets from suppliers. In addition, bio-fillers are recovered from agricultural waste and dried. Thus, it was assumed that no biofilm formation would occur. The only concern for the bio-filler, as well as mined calcite, as raw materials used for the bio-composite production, is about the chemical contamination. The safety data sheets identify the main hazards and associated risks related to the use of these materials, including instructions that need to be followed for the preparation and handling. However, mined calcite, bio-fillers, and resins may contain chemicals classified as hazardous to human health. Therefore, all the raw materials, except for resins, were analysed for heavy metals using inductively coupled plasma mass spectrometry (ICP-MS) and atomic fluorescence spectroscopy (AFS). For this purpose, samples were made from all available batches of raw materials. For example, calcite is delivered in several bags, and a quantity of about 30 g of material was collected from each bag of each raw material to prepare the sample for analysis. Samples were prepared by filtration through a microfilter with a pore size of 0.45 μm, followed by acidification with nitric acid prior to analysis. Determination of mercury (Hg) was performed with a fluorescence spectrometer following the standards US EPA 245.7 and EN ISO 17852. Other elements were measured using the ICP-MS technique following the standards US EPA 200.8, EN ISO 17294-2, US EPA 6020A, and CSN 75 7358. The ICP-MS was carried out in an accredited external laboratory. The obtained results are presented in Table S1 of the Supplementary material.

The ICP-MS results are used for quantitative risk assessment. The resins are addressed by means of safety data sheets from which it is possible to calculate the amount of styrene and furfuryl alcohol for polyester and furan resin, respectively, based on the composition of the bio-composite.

The risk assessment is based on the worst-case scenario: no PPE and safety protocols are used in the bio-composite production process. The mixing phase is the object of this study, where the workers are exposed to the dust generated by the raw materials and to the resins. The quantitative risk assessment is described in section 2.2.2.

2.2.2. Quantitative risk assessment

The risk map produced in the previous step was used as a basis for the quantitative risk assessment. As shown in Figure 1, the risks are human health risks related to the presence of chemical and microbial contaminants in the raw materials. Therefore, the quantitative chemical risk assessment (QCRA) and the quantitative microbial risk assessment (QMRA) methods are used here to quantify different aspects of human health risk.

2.3. Quantitative chemical risk assessment

QCRA is performed according to the USEPA method (E.P.A. 2022). The QCRA is structured as follows:

1. Hazard identification: chemicals with the potential to cause harm to humans (e.g., workers) have been detected at this stage. In this phase, the stressors such as heavy metals (e.g., arsenic, cadmium, chromium, lead, etc.), styrene, and furfuryl alcohol are identified.
2. Dose–response: this stage evaluates the numerical relationship between the stressor and the human response, which defines the effects.
3. Exposure assessment: this stage characterizes the exposure based on the concentration of the stressors. Then the exposure routes through which the exposure occurs are defined, such as indoor or outdoor environment, and exposure duration.

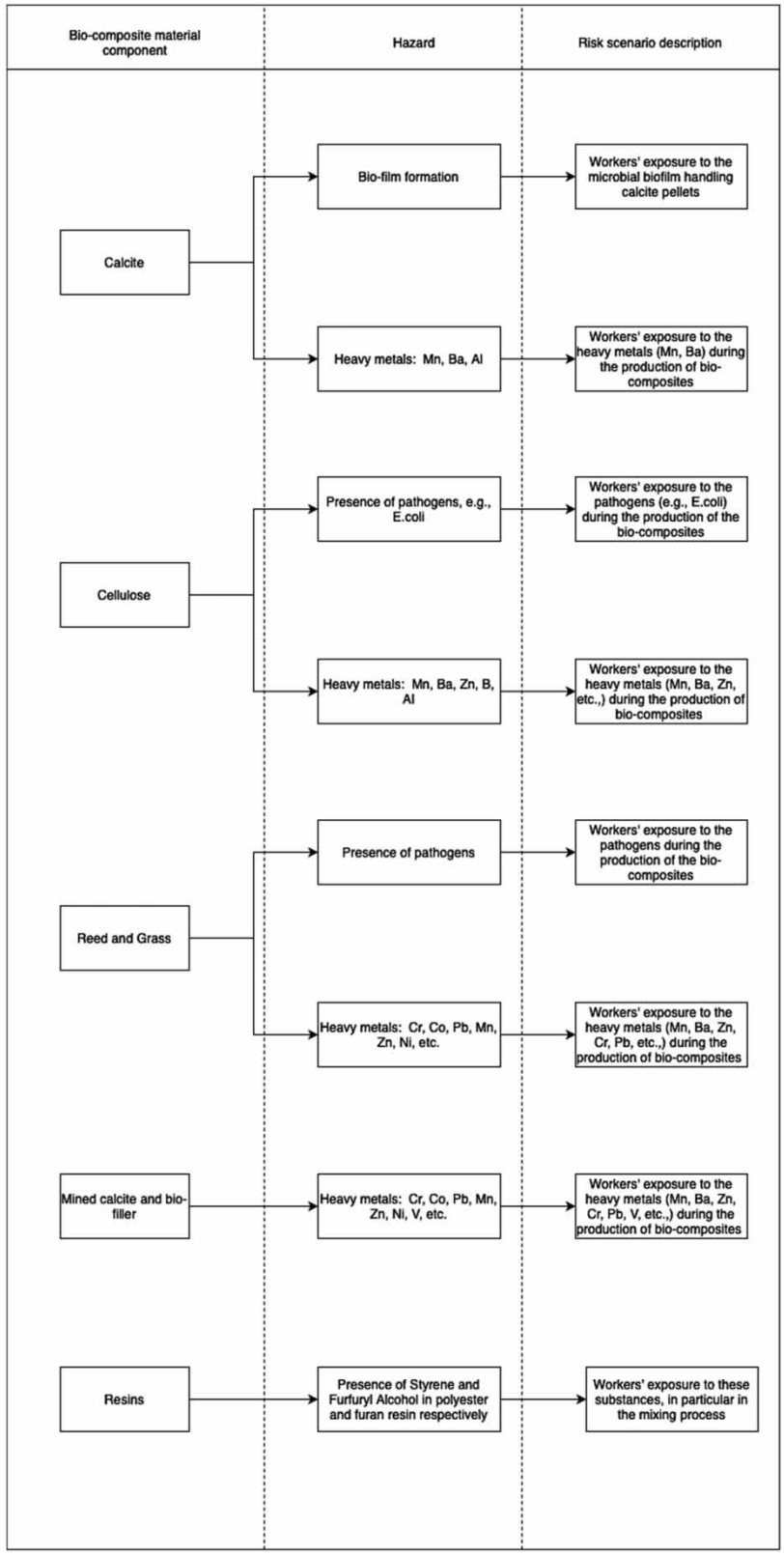


Figure 1 | Risk map as the result of the qualitative risk mapping for bio-composite material production process.

4. Risk characterization: in this stage, the level of risk is determined, which consists of (i) risk estimation and (ii) risk description. The first concerns the estimation or measurement of the level of exposure for each stressor. The second is used to interpret the results: adverse effects, uncertainties, reasonable alternative interpretations, etc.

The framework is described in the handbooks published by USEPA (U.S.E.P.A. 1989, 2009).

In this work, the object is the quantitative risk assessment due to the presence of heavy metals and toxic/dangerous chemicals such as styrene and furfuryl alcohol. In particular, chemical exposure may result in non-cancer and cancer-type risks, based on the chemical properties of the chemicals present in the raw materials. The classification as hazardous chemical is available in the literature and published by USEPA-IRIS (U.S.E.P.A. IRIS 2023).

In this work, the QCRA aims to determine whether the levels of chemicals present in the raw materials, and subsequently in the bio-composite material, could adversely affect human health for a given exposure scenario. As mentioned earlier, exposure was assumed to occur by accidental ingestion, inhalation, and/or dermal contact with the contaminated dust generated from the raw materials during the mixing process. The exposure dose was calculated according to the guidelines published by U.S.E.P.A. (1989).

The U.S.E.P.A. Handbook (U.S.E.P.A. 2011d) provides literature data concerning human exposure to contaminated soil and dust for different age groups and genders. The relevant parameter values may vary depending on the scenario in which the framework is applied. For example, the exposure during the bio-composite production occurs in an indoor environment for one working day (8 h/day) in the range of 200–300 days/year with an average value of 250 days/year. The other input parameters such as ingestion, inhalation rate, available skin area, and body weight are also available in the U.S.E.P.A. (2011d) Handbook. Several parameters, such as ingestion, inhalation rate, adherence factors, body weight, and available skin area, are selected in a range between the ages of 21 and 61 years of age for both male and female groups. An average value is then calculated for each parameter and used to apply the deterministic approach of the QCRA to assess the exposure and the final human health risk.

Given the uncertainty present in many of the input values for the QCRA method, a sensitivity analysis was performed to analyse how different values of the input variables (e.g., chemical concentration, body weight, ingestion rate, etc.) may affect the risk index of each chemical and the bio-composite material. The sensitivity analysis is performed using the Monte Carlo method and described in Section 2.2.4.

2.4. Non-cancer risk assessment

Non-cancer risk, defined by calculating the hazard quotient (HQ) and hazard index (HI) (E.P.A. 2023), includes acute, sub-chronic, and chronic effects based on the exposure scenario and chemical properties. The HQ (ratio between the exposure dose and the reference allowable dose at which no adverse effects are likely to occur (U.S.E.P.A. 2022)) and HI (the sum of the HQs of chemicals to which a person is exposed (U.S.E.P.A. 2023)) are generally used as indicators of the likelihood of harm resulting from the non-cancer effects of chemicals (Asante-Duah 2017). The value of HI below the threshold value of 1.00 (U.S.E.P.A. 1989) is generally considered to be an acceptable risk. In contrast, values above 1.00 would indicate a likely negative effect. However, by definition (U.S.E.P.A. 2023) the HI is only qualitatively related to the likelihood of adverse effects. Therefore, neither the HI nor the HQ can be translated into a probability of the occurrence of adverse effects. However, the HI and HQ still represent the non-cancer risk, not in terms of probability but in qualitative terms (U.S.E.P.A. 1989, 2023).

To calculate the HQ for each exposure route, the resulting exposure assessment is compared with the reference doses (RfDs). Reference doses are specific to each exposure route and represent the maximum allowable dose of a toxic substance at which no adverse health effects are expected to occur from a lifetime exposure (U.S.E.P.A. 2022). The RfDs vary according to the duration of exposure, such as acute, sub-chronic, and chronic. In this risk assessment framework, chronic exposure is considered. Chronic exposure is repeated exposure to a toxic substance over a long period of time (months or years). Chronic exposure is defined as when chemicals are used every day at work, so that workers are exposed to these chemicals every day.

The RfD values (for ingestion, inhalation and dermal contact) are obtained from the safety data sheets for each chemical provided by I. U.S.E.P.A. (2023) and from several public databases such as the Risk Assessment Information System, Informative Furan Chemicals and the Screen Regional Level (RSL 2020; IFC 2022; RAIS 2023). The RfDs for both dermal and inhalation exposure for chemicals for which data are not directly available in the literature are calculated as follows:

1. Dermal exposure: the reference value (RfD_{derm}) is calculated using the reference dose for ingestion exposure (RfD_{ing} [mg/kg/day]) and the gastrointestinal absorption factors (GIABS) [–]. The latter was collected for each chemical from the standard and guidelines database (RSL 2020; IFC 2022; RAIS 2023). The gastrointestinal adsorption factor represents the rate at which a chemical is absorbed in the gastrointestinal tract of the human body. This value is divided between the skin and a solid medium, for example, dust (RAIS 2022a). The dermal reference dose is calculated as follows:

$$RfD_{derm} = RfD_{ing} * GIABS \quad (1)$$

2. Inhalation exposure: the reference value (RfD_{inh}) for inhalation exposure is derived from the reference concentration (RfC) (mg/m^3) (U.S.E.P.A. 2009; RAIS 2022a). The RfC is defined as the concentration inhaled over a continuous inhalation exposure (acute, chronic, or sub-chronic) to a chemical at which no adverse effects are expected to occur (E.P.A. 2023). The RfD for inhalation exposure is calculated as follows (RAIS 2022b):

$$RfD_{inh} = \frac{RfC * InhR}{BW} \quad (2)$$

where InhR is the inhalation rate (m^3/day) and BW is the average body weight for adults (kg).

The HQ is calculated separately for each chemical and exposure route. The HI for a chemical is then calculated as the sum of all HQs for that chemical. The overall HI value for a bio-composite material is calculated as the sum of all HIs for all chemicals present in the material. The overall HI value represents the human health risk associated with the analysed bio-composite material during its production. This value obtained this way is then compared with the threshold value of 1.00 for non-cancer risk (U.S.E.P.A. 1989). If the value obtained is less than 1.00, the risk is considered acceptable. Otherwise, safety measures must be taken.

2.5. Cancer risk assessment

Cancer risk (CR) is calculated by considering the long-term (lifetime) effects as recommended by standard guidelines (U.S.E.P.A. 2005) as an appropriate measure of exposure to a carcinogen. The CR is defined by the probability that a person will develop cancer over a lifetime as a result of exposure to one or more carcinogens (Asante-Duah 2017). The CR is calculated by multiplying the calculated exposure (for different exposure routes) by the cancer slope factor. The slope factor is defined as the upper 95% confidence limit of the probability of developing cancer over a lifetime exposure (Asante-Duah 2017). Further details on the calculations and formulae for both non-cancer and cancer risk are provided in the Supplementary Material.

Some of the chemicals are also known human carcinogens. The cancer risk is assessed according to the standard U.S.E.P.A. guidelines (U.S.E.P.A. 2005). As explained earlier, to assess the cancer risk, the average lifetime (e.g., 70 years) has to be taken into account, as cancer risk is a long-term effect. To calculate the cancer risk for each exposure, the slope factors (SFs) for ingestion and inhalation are obtained from the above-mentioned RfDs databases (RSL 2020; IFC 2022; RAIS 2023).

The dermal cancer slope factor is derived from the ingestion cancer slope factor, as follows (NJDEP 2021; RAIS 2023):

$$SF_{derm} = SF_{ing} * GIABS \quad (3)$$

where SF_{ing} is the ingestion cancer slope factor $(mg/kg*day)^{-1}$. The cancer risk is then calculated in a similar way to the non-cancer risk. Detailed calculations can be found in the Supplementary Material. The overall cancer risk index (CRI) is compared with the threshold value of 1×10^{-6} for that risk (U.S.E.P.A. 2005). If the CRI obtained is below the threshold, the risk can be considered acceptable.

Table 2 lists the RfDs and SFs used for dose–response model calculations.

2.5.1. Quantitative microbial risk assessment

The aim of QMRA is to investigate the risk that could be posed to human health by the presence of pathogens in the raw materials. Literature data (Heuvel 2019) were used in the calculations to perform the QMRA assessment. Data from untreated cellulose fibres were chosen as the worst-case scenario.

Table 2 | RfD and SF values collected from USEPA database (RSL 2020; IFC 2022; RAIS 2023)

Element	RfD mg/kg/day	RfDoral mg/kg/day	RfC mg/m³	GIABS –	RfDderm mg/kg/day
Si	0.00×10^{0}	6.14×10^{-4}	3.00×10^{-3}	0.00×10^{0}	0.00×10^{0}
Al	1.00×10^{0}	1.02×10^{-3}	5.00×10^{-3}	1.00×10^{0}	1.00×10^{0}
Fe	7.00×10^{-1}	0.00×10^{0}		0.00×10^{0}	0.00×10^{0}
Mg	1.10×10^{-1}	2.05×10^{-2}	1.00×10^{-1}	1.00×10^{0}	1.10×10^{1}
Na	1.90×10^{1}	0.00×10^{0}		1.00×10^{0}	1.90×10^{1}
Ti	3.00×10^{0}	0.00×10^{0}		0.00×10^{0}	0.00×10^{0}
P	4.90×10^{1}	0.00×10^{0}		1.00×10^{0}	4.90×10^{1}
Be	2.00×10^{-3}	4.09×10^{-6}	2.00×10^{-5}	7.00×10^{-3}	1.40×10^{-5}
Cr	3.00×10^{-3}	2.05×10^{-5}	1.00×10^{-4}	2.50×10^{-2}	7.50×10^{-5}
Co	3.00×10^{-4}	1.23×10^{-6}	6.00×10^{-6}	1.00×10^{0}	3.00×10^{-4}
Pb	4.00×10^{-3}	0.00×10^{0}		0.00×10^{0}	0.00×10^{0}
Mn	2.40×10^{-2}	1.02×10^{-5}	5.00×10^{-5}	4.00×10^{-2}	9.60×10^{-4}
Mo	5.00×10^{-3}	4.09×10^{-4}	2.00×10^{-3}	1.00×10^{0}	5.00×10^{-3}
Ni	1.10×10^{-2}	2.87×10^{-6}	1.40×10^{-5}	4.00×10^{-2}	4.40×10^{-4}
V	5.04×10^{-3}	2.05×10^{-5}	1.00×10^{-4}	2.60×10^{-2}	1.31×10^{-4}
Zn	3.00×10^{1}	0.00×10^{0}		1.00×10^{0}	3.00×10^{-1}
Ba	2.00×10^{-1}	1.02×10^{-4}	5.00×10^{-4}	7.00×10^{-2}	1.40×10^{-2}
B	2.00×10^{-1}	4.09×10^{-3}	2.00×10^{-2}	1.00×10^{0}	2.00×10^{-1}
Li	2.00×10^{-3}	0.00×10^{0}		1.00×10^{0}	2.00×10^{-3}
Sn	6.00×10^{-1}	0.00×10^{0}		1.00×10^{0}	6.00×10^{-1}
Bi	0.00×10^{0}	0.00×10^{0}		0.00×10^{0}	0.00×10^{0}
Styrene	2.00×10^{-1}	1.84×10^{-1}	9.00×10^{-1}	1.00×10^{0}	2.00×10^{-1}
Furfuryl alcohol	7.57×10^{-4}	1.25×10^{-3}	6.09×10^{-3}	1.00×10^{0}	7.57×10^{-4}

QMRA is carried out according to the W.H.O. guidelines (Ashbolt 2005; W.H.O. 2016). The methodology is structured as follows:

1. Problem formulation: this step defines the purpose and the scope of the investigation. This step includes hazard identification (selection of reference pathogens based on local conditions, source water characteristics, and incidence and severity of waterborne disease).
2. Exposure assessment: in this stage, exposure is characterized by defining and quantifying the exposure pathways. The exposure is then characterized by quantifying the severity and frequency of exposure based on the case study.
3. Health effects assessment: in this step, the health effects are assessed by collecting the health effects data for the identified hazards and the specific study population. This step includes the dose–response model, the probability of illness, and the burden of disease.

    3.1. Dose–response: this step consists of identifying the relationship between exposure to the agent and the estimated effects (either infection or disease). A model must be selected from the literature database (Q.M.R.A.Wiki 2017).
    3.2. Probability of illness: people can be infected by pathogens without showing symptoms. Thus, when using an infection-based dose–response model, it is important to consider the probability of illness once infected (W.H.O. 2016).
    3.3. Burden of disease: the metric used in the W.H.O. guidelines is disability-adjusted life years (DALY). This measure is expressed per person per year (pppy).

4. Risk characterization: Exposure and health effects assessments are combined, and calculations are made to quantify and characterize risk.

To assess the microbial risk, the main potential pathogens such as *Escherichia coli* and *Clostridium* that may be present in cellulose fibres collected from wastewater (Heuvel 2019) and incidentally ingested through the hand-mouth route from workers' hands (or gloves) during the bio-composite production are considered here. The dose–response models specific to each pathogen were obtained from the QMRA database (Q.M.R.A.Wiki 2017). The dose–response analysis provides a relationship (quantitative) between the probability of adverse effects and the level of microbial exposure (severity). This is fundamental as input data for risk characterization. The risk characterization combines the dose–response model and the exposure assessment to estimate the level of microbial risk, and the uncertainties. The uncertainties of this model are related to the level of measured pathogen concentration. Furthermore, disinfection treatments of raw materials prior to their use in bio-composite production are not precise in terms of pathogen reduction.

The amount of the fraction ingested may vary due to human factors (changing of gloves, washing hands, taking care not to touch the face during the mixing process, etc.) which are not predictable. The exposure scenario used in the guidelines (W.H.O. 2016) is based on accidental ingestion of contaminated food due to the use of contaminated surface water or wastewater for irrigation. Thus, the exposure assessment is modified based on the bio-composite production process. The input parameters must be suitable for the case study. Therefore, based on the available data and the bio-composite production scenario, only the ingestion route is considered in the QMRA. No data are available for taking into account inhalation and dermal contact routes. The ingestion rate is defined as in the QCRA, with a value of 0.03 g/day, taking into account the accidental ingestion of contaminated dust. The exposure duration in this case is also considered to be 8 h/day (working day) for an average of 250 days/year for the indoor environment as exposure frequency.

2.5.2. Sensitivity analysis

The input data for the risk assessment were collected from the literature (Delli Compagni *et al.* 2020; Dehghani *et al.* 2022; Selvam *et al.* 2022) and interviews with industry experts involved in water resource recovery processes. As many of these input parameters are uncertain, sensitivity analysis using Monte Carlo method (Johansen 2010) was carried out to assess the impact of these uncertainties on the estimated human health risks. The following five cases are analysed in the assessment of chemical and microbial risks:

1. Sensitivity case 0 (s0): the concentrations of chemicals (QCRA) and pathogens (QMRA) detected in raw materials are simulated using a uniform distribution. The uniform distribution is used as an approximation where little or no data are available.
2. Sensitivity case 1 (s1): exposure rate parameters such as ingestion rate, inhalation rates, and skin area are simulated using a lognormal distribution, as suggested by the USEPA Handbook (U.S.E.P.A. 2011d). Different values are chosen for each parameter depending on the age and gender. The geometric mean and standard deviation values are calculated for the inhalation rate and the available skin area for the head and hands. Concerning the ingestion rate, only a single value for dust ingestion is available in the literature, so the 96% confidence interval is used as the standard deviation. With regard to the QMRA model, only the ingestion route is considered, as described in Section 2.2.3. Therefore, only the ingestion rate is simulated as done for the QCRA.
3. Sensitivity case 2 (s2): the exposure frequency is modelled using the lognormal distribution (U.S.E.P.A. 2011d). The exposure frequency considered is for 200, 250, and 300 days/year. The average value of 250 days/year is calculated and the 96% confidence interval is used as the standard deviation. This model is the same for both QCRA and QMRA.
4. Sensitivity case 3 (s3): for QCRA, body weight is simulated using a lognormal distribution as above. The parameters for the distribution are gender based. The geometric mean and standard deviation are calculated. For QMRA, body weight is not an input parameter for QMRA. Thus, this case of sensitivity analysis is not included in the QMRA stochastic approach.
5. Sensitivity case 4 (s4): all input parameters are simulated simultaneously as uncertain to evaluate the maximum acceptable risk. This case is represented as 's3' for QMRA.

The input parameters used for both the QCRA and QMRA sensitivity analyses, simulated using Monte Carlo method, are listed in Table 3. The number of trials is chosen based on the stability of the output achieved. The procedure of selecting the number of trials is carried out by iteration. Different numbers of trials are tested such as 10,000, 20,000 50,000, and 100,000 trials. The stability of the outputs is reached from 10,000 trials.

Table 3 | Input parameters for sensitivity analysis

Input parameter	Unit	Mean	Standard deviation	Distribution	References
Chemical concentration	mg/kg	Experimental value		Uniform	
Ingestion rate	mg/day	0.03	1.2	Lognormal	U.S.E.P.A. (2011a)
Inhalation rate	m^3/day	15.52	0.753	Lognormal	U.S.E.P.A. (2011b)
Skin surface area hands	cm^2	980	127.3	Lognormal	U.S.E.P.A. (2011c)
Skin surface area head	cm^2	1	155.56	Lognormal	
Exposure frequency	day/year	250/365	0.0274	Lognormal	U.S.E.P.A. (2011d)
Body weight	kg	75.6	5.94	Lognormal	
Pathogen concentration	CFU/mL	Experimental values		Uniform	

CFU, colony forming units.

3. RESULTS AND DISCUSSION

3.1. QCRA results

The QCRA was first carried out using a conventional (deterministic) approach, and then a stochastic approach to assess the impact of the above uncertainties.

The results of the deterministic approach for chemical risk assessment per 1 kg of material are presented in Table 4. Observing the non-cancer HI, all values are below the threshold value of 1.00 for all four materials, leading to an overall HI as acceptable risks. The highest HI is obtained for dermal exposure. The production of bio-composites involves the manipulation of raw materials, in particular resins, to obtain a uniform mixture which is then pressed to produce bio-composite panels. The raw materials used in this process tend to generate dust, making dermal exposure the most likely route during the mixing phase. This dust can potentially settle on hair, clothing, and hands, posing a risk of dermal contact also after the mixing stage.

CRI shows values above the threshold value of 1.0×10^{-6}. Also, in this case, dermal contact is the major contributor to the overall risk for the reasons given earlier.

The results presented in Table 4 are graphically presented in Figure 2, highlighting the chemicals with the most significant contributions to the overall non-cancer risk for the four bio-composite materials studied. The predominant heavy metal contributing to the overall HI for all four alternatives is manganese (Mn). This significant contribution is a result of the noticeable amount of manganese present in most of the raw materials, excluding reeds. This high prevalence of manganese in the raw

Table 4 | QCRA results for all four materials in terms of non-cancer hazard index (HI) and cancer risk index (CRI)

Material	Exposure routes	Non-cancer hazard index (HI)	Cancer risk index (CRI)
M1	Accidental dust ingestion	5.03×10^{-4}	4.66×10^{-7}
	Dust inhalation	4.18×10^{-7}	9.42×10^{-13}
	Dermal contact	6.93×10^{-3}	6.15×10^{-6}
	Total	$\mathbf{7.40 \times 10^{-3}}$	$\mathbf{6.61 \times 10^{-6}}$
M2	Accidental dust ingestion	3.53×10^{-4}	3.26×10^{-7}
	Dust inhalation	2.59×10^{-7}	5.23×10^{-13}
	Dermal contact	4.82×10^{-3}	4.29×10^{-6}
	Total	$\mathbf{5.20 \times 10^{-3}}$	$\mathbf{4.26 \times 10^{-6}}$
M3	Accidental dust ingestion	3.65×10^{-4}	3.38×10^{-7}
	Dust inhalation	3.06×10^{-7}	5.41×10^{-13}
	Dermal contact	5.00×10^{-3}	4.45×10^{-6}
	Total	$\mathbf{5.40 \times 10^{-3}}$	$\mathbf{4.79 \times 10^{-6}}$
M4	Accidental dust ingestion	5.10×10^{-3}	5.78×10^{-8}
	Dust inhalation	4.76×10^{-7}	1.14×10^{-12}
	Dermal contact	6.71×10^{-2}	2.42×10^{-6}
	Total	$\mathbf{7.20 \times 10^{-2}}$	$\mathbf{2.48 \times 10^{-6}}$

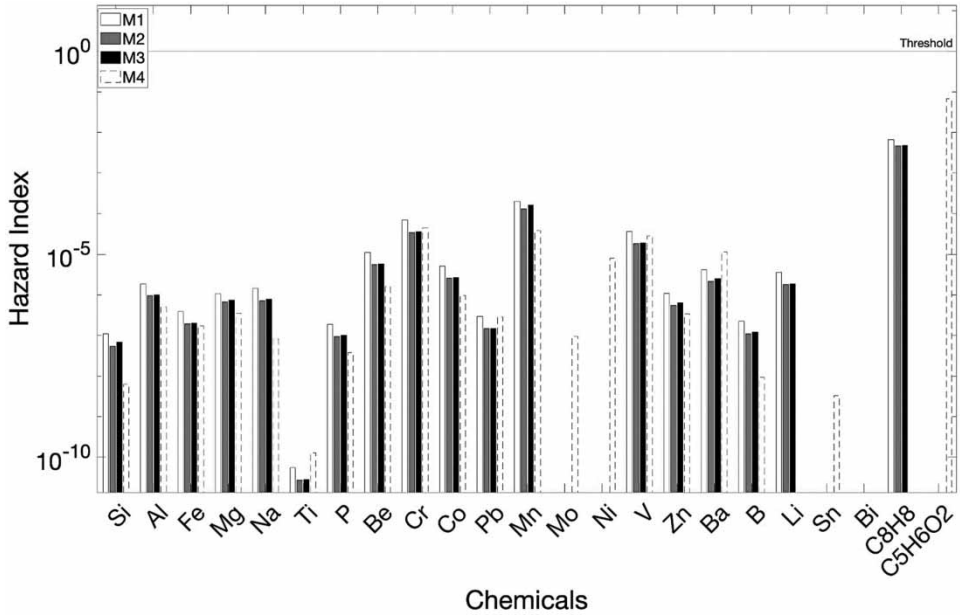


Figure 2 | Comparison of non-cancer risk index for all four bio-composite materials.

materials is the main reason for its significant influence on the HI for heavy metals in all four materials. Furthermore, chromium (Cr) and vanadium (V) play a significant role in the non-cancer risk, especially for the M1 and M4 alternatives. The increased contribution of these two elements can be directly related to their detection in mined calcite, which accounts for a larger proportion of M1, and in grass, which is used as a natural fibre for M4, as shown in Table 1. These results underline the significant influence of the initial chemical composition of the raw materials on the risks to human health, including both non-cancer and cancer risk assessments. Interestingly, chromium emerges as the major contributor to cancer risk for heavy metals M1 and M4 (Figure 3), which is consistent with the above observations for non-cancer risk. In particular,

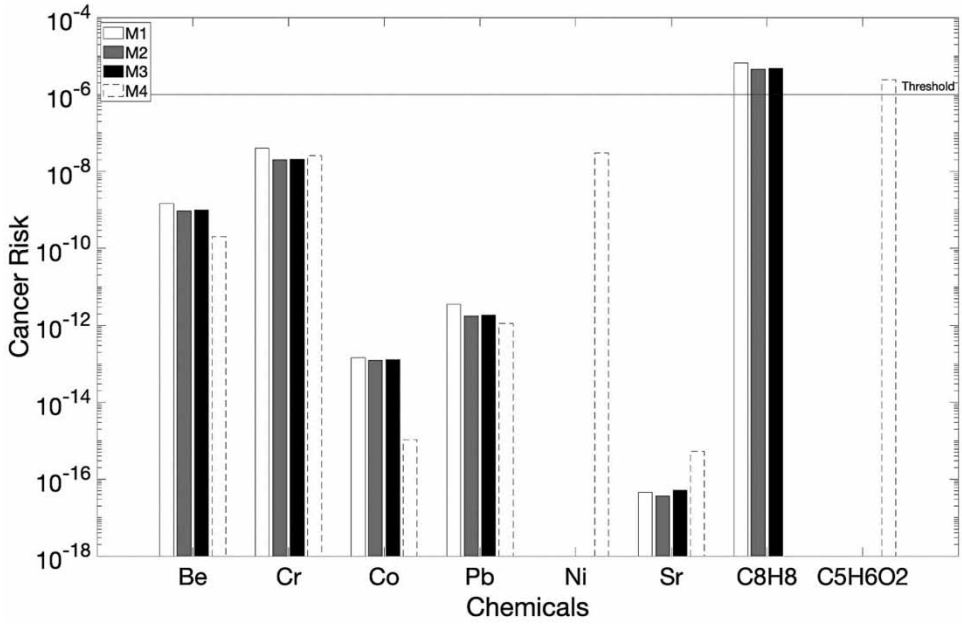


Figure 3 | Comparison of cancer risk for all four bio-composite materials.

material M4 approaches the critical threshold of 1.00 for total non-cancer risk, mainly due to the presence of furfuryl alcohol in the furan resin.

Furfuryl alcohol poses a significant risk to human health in both non-cancer and cancer-related contexts. For materials M1, M2, and M3, styrene stands out as the main chemical contributing to the overall non-cancer risk. This hazardous chemical is commonly found in polyester resins. Similarly, furfuryl alcohol, known for its volatility and adverse effects on human health, contributes significantly to the non-cancer and cancer risks. Furthermore, heavy metals such as manganese (Mn), chromium (Cr), vanadium (V), barium (Ba), and beryllium (Be) play a key role in the non-cancer risk indices, affecting the overall non-cancer risk in all four bio-composite alternatives. Notably, these elements (as detailed in Table S1 of the Supplementary Material) are detected in grass and mined calcite, resulting in higher hazard quotients and, consequently, hazard indices for materials M1 and M4.

It would be interesting to investigate the specific preparation treatments of the raw materials prior to their reuse in bio-composite production. Knowledge of the specific preparation treatment may help to define whether the metals mentioned earlier are the result of contamination due to the preparation treatments, or whether they were present where the raw materials were collected. Furthermore, chemical treatment to remove heavy metals may be carried out before the raw materials are reused. The calculations have been made by considering 1 kg of bio-composite material (pilot scale). Thus, in the real case, the exposure might be higher because a higher quantity of raw materials is handled, which increases the exposure. Therefore, safety measures must be taken to protect the health of the workers, such as the use of specific PPE when handling raw materials, especially resins.

Concerning the cancer risk (Figure 3), as mentioned earlier, the risk level is above the threshold for all four materials due to the presence of styrene and furfuryl alcohol. As is done for non-cancer risk, the assessment is carried out by considering 1 kg of bio-composite product (pilot scale). Furthermore, the amount of styrene and furfuryl alcohol is assumed based on safety data sheets from resin suppliers. As mentioned earlier, both styrene and furfuryl alcohol are dangerous to human health and are defined as carcinogens.

In order to get more precise results, the sensitivity analysis by using Monte Carlo method has been carried out as described in Section 2.2.4.

The findings of the sensitivity analysis for non-cancer and cancer risks are shown in Figures 4 and 5, respectively. The analysis includes all four materials analysed and for the sensitivity case s4, in which all input parameters are modelled simultaneously using the Monte Carlo method. The boxplots in these two figures represent the risk values for the 25th and 75th percentiles. The horizontal line inside the box plot represents the median (50th percentile) and the signs '+' and '−' represent the minimum and maximum values obtained. The signs '+' and '−' are visible only for s1, s2, and s3 cases

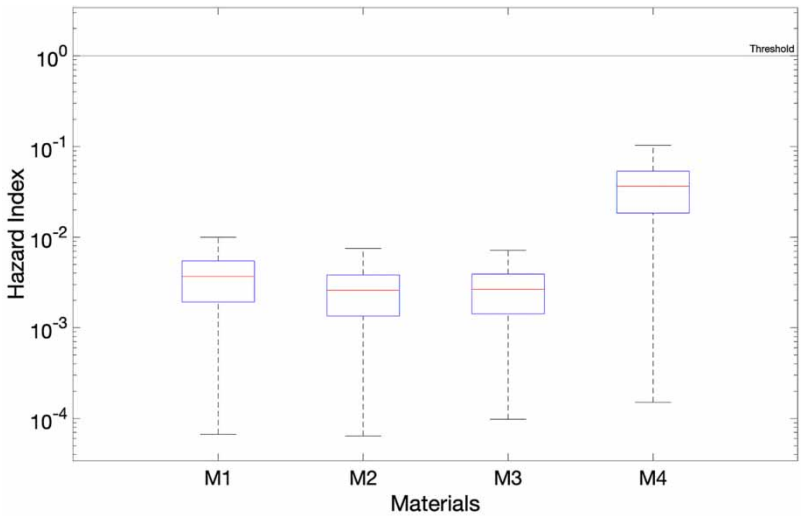


Figure 4 | Comparison of total non-cancer risk for all materials based on sensitivity case s4. The boxplots represent the risk values for the 25th and 75th percentiles. The horizontal line inside the box plot represents the median (50th percentile) and the signs '−' represent the minimum values obtained.

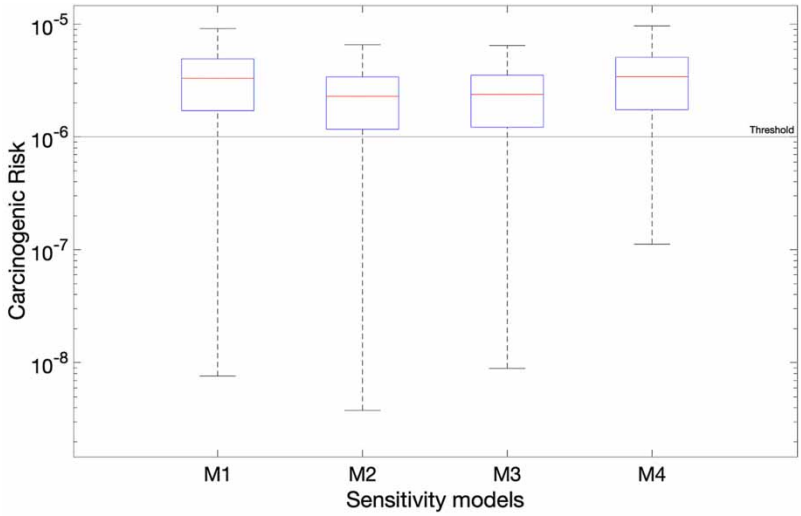


Figure 5 | Comparison of total cancer risk index for all materials based on sensitivity case s4. The boxplots represent the risk values for the 25th and 75th percentiles. The horizontal line inside the box plot represents the median (50th percentile) and the signs ' − ' represent the minimum values obtained.

(shown in Figures 6 and 8), where the uncertainty is higher due to the narrow range of the boxplot obtained with these simulations.

Figures 4 and 5 show that the overall risk level varies between different materials, but the risk level is always below the threshold for the non-cancer risk and above the threshold for cancer risk for most uncertain samples. The simultaneous consideration of all input parameters in our simulations results in a remarkably wide range of output values, especially when assessing the overall risk for both non-cancer and cancer risks. Material M4 has the highest risk index for non-cancer risk, confirming the results of our deterministic approach. This increased risk level is mainly due to the presence of furfuryl alcohol, which is the largest single contributor to the overall risk in this context. It is interesting to note that when examining the maximum value obtained from the sensitivity analysis (especially the s4 case) for the M4 material, the resulting risk is very close to the results obtained from the deterministic approach. This similarity underlines the robustness and consistency of the obtained results. Finally, the analysis performed underlines the central role of the initial chemical composition of the

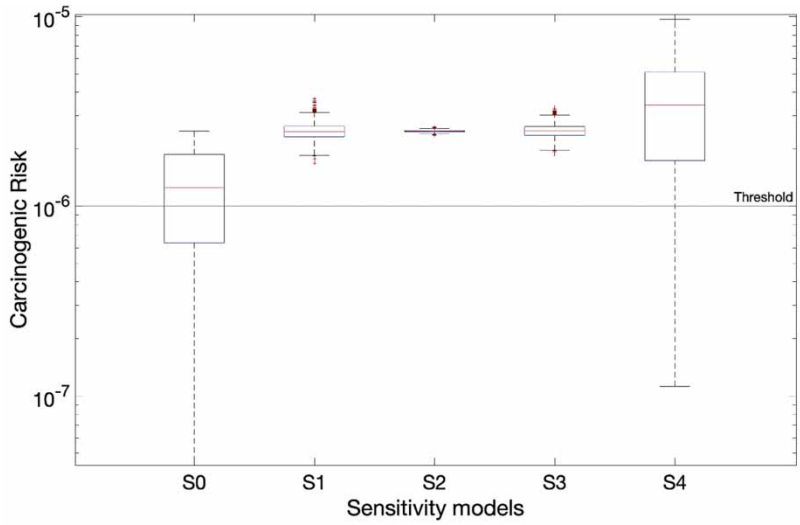


Figure 6 | M4 sensitivity model comparison. The boxplots represent the risk values for the 25th and 75th percentiles. The horizontal line inside the box plot represents the median (50th percentile) and the signs ' + ' and ' − ' represent the minimum and maximum values obtained.

materials. This factor emerges as the most critical determinant in the context of QCRA. In other words, the initial chemical content of materials is the key parameter that significantly influences the risk associated with both non-cancer and cancer risks.

The overall risk for all four materials is above the threshold. This is due to the presence of styrene and furfuryl alcohol in polyester and furan resin, respectively. These two substances are toxic to human health for both non-cancer and cancer risk. The assessment of cancer risk must take into consideration lifetime exposure, which is a longer period of exposure than non-cancer risk. The cancer potency factors and unit risk factors are estimated using long-term data from epidemiological studies (OEHHA 2012). Furthermore, these compounds pose a greater risk of causing cancer rather than non-cancerous risks. PPE and safety protocols are therefore essential to reduce the exposure.

Materials M1, M2, and M3 are made from polyester resin containing styrene. M1 has a slightly higher non-cancer and cancer risk level than M2 and M3, due to the higher amount of styrene in the resin. Material M4 has the highest non-cancer and cancer risk due to its composition with furan resin, which contains furfuryl alcohol.

Figure 6 shows the cancerogenic risk trend of M4 for all sensitivity cases.

As can be seen in this figure, the widest range of risk values (100-fold) is obtained in the s0 case with many uncertain risk values below the threshold. This can be attributed to the large variation in the modelled concentration of all the heavy metals detected in the raw materials by ICP-MS analysis. This indicates that the measured values of chemical contaminants have the greatest influence on the width of the risk interval, and therefore monitoring of the raw material quality and the use of large datasets for the risk assessment are recommended. This result confirms that the original chemical composition of the material is the most influential parameter in terms of overall risk.

The narrowest range between the minimum and maximum risk values, observed in case s2, indicates that the frequency of exposure has a minimal effect on the overall risk. The distributions of the cancer risk values in cases s1 and s3 are also rather narrow. These variations are attributed to the simulation of ingestion, inhalation rate, skin surface area, and body weight, respectively. This demonstrates that when risk assessment relies on average data that do not consider physical variations, such as differences in body weight or skin surface area, there is a possibility of underestimating or overestimating the risk by a small margin (1–2-fold). The input parameters simulated in cases s1, s2, and s3 are selected on the basis of the USEPA handbooks (U.S.E.P.A. 2011d). The selected values for each input parameter differ from each other by a small interval. Thus, unlike the chemical concentrations in case s1, a large variation cannot be observed between the minimum and maximum values of each input parameter. The chemical concentrations are based on observed values, therefore the largest range between minimum and maximum values is reached in case s0 and not in other cases.

In model s4, all input parameters were simulated simultaneously. Concentrations of chemical contaminants influenced the wide range of results that spans over 50-fold, while other parameters influenced the average overall risk. Based on the results obtained from both deterministic and stochastic approaches, the cancer risk levels are above the threshold. Appropriate PPE must therefore be used. This highlights the importance of human health risk assessment, not only for these four particular biocomposites, but for all novel materials.

3.2. QMRA results

Only the data related to cellulose fibres were available in the literature about microbial contamination; hence, only material M3 was analysed. The obtained results from the deterministic model are shown in Figure 7.

Figure 7 shows that *E. coli* is the only pathogen of concern for material M3. The effectiveness of the disinfection treatments of raw materials after recovery is unknown. Thus, as worst-case scenario, for this QMRA application, the observed data published by Heuvel (2019) of raw cellulose fibres (untreated) recovered from a wastewater treatment plant were considered.

The microbial risk results obtained tend to overestimate the actual microbial risk when untreated cellulose fibres recovered from wastewater are considered. At this stage, the cellulose fibres are inevitably contaminated with a variety of pathogens, a contamination profile that is closely linked to the characteristics of the wastewater source. To prepare these cellulose fibres for reuse, they are subjected to a drying and heating process at elevated temperatures, the main aim of which is to significantly reduce the number of pathogens present. It is important to note that this paper does not deal with the specifics of the disinfection treatments applied to the raw materials, nor with the quality of the water from which these materials are recovered. However, the disinfection treatment of raw materials, particularly in the case of cellulose fibres, plays a key role in reducing the microbial risk to human health. For a more comprehensive assessment of microbial risk, it is essential to consider the disinfection process of raw materials and the quality of the water sources from which these materials are derived. Proper

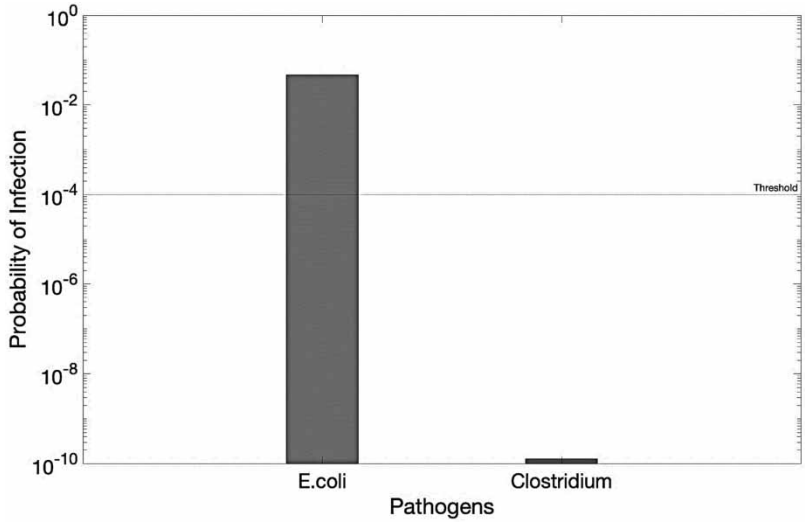


Figure 7 | Deterministic results of QMRA model carried out on material 3 (M3).

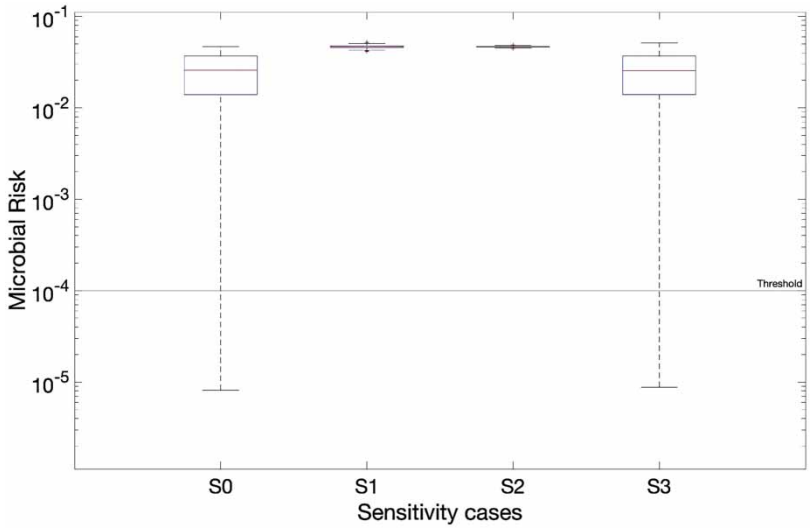


Figure 8 | Microbial risk results for material 3 (M3). The boxplots represent the risk values for the 25th and 75th percentiles. The horizontal line inside the box plot represents the median (50th percentile) and the signs '+' and '−' represent the minimum and maximum values obtained.

disinfection protocols are an integral part of ensuring the safety and suitability of recovered cellulose fibres and other materials for various applications. This includes not only the removal of pathogens, but also the maintenance of the desired quality standards for the end product in accordance with health and safety regulations.

As explained earlier, the original amount of pathogens is the most uncertain parameter in the study. Thus, the sensitivity analysis was performed as in QCRA.

Pathogen concentrations were simulated using a uniform distribution to assess the risk at the lowest and highest concentrations. The results of the sensitivity analysis are shown in Figure 8.

QMRA sensitivity analysis provides remarkable insights into the microbial risk associated with different cases. The widest range of microbial risk values is observed for case s0, highlighting the considerable variability in the results. This variability is mainly driven by variations in pathogen concentration, a parameter with the greatest influence on model output. As discussed in previous sections, it is advisable to use larger datasets for risk assessment in cases such as this, as pathogen concentrations contribute significantly to the observed wide range of results, spanning more than 10×10^5-fold.

Similarly, in case s3, where all input parameters are simulated simultaneously, a considerable range of risk values, was observed indicating the complex interplay between these factors in microbial risk assessment. Conversely, in cases s1 and s2, where parameters such as ingestion rate and exposure frequency are modelled explicitly, the impact on microbial risk appears to be relatively minimal. This is evident from the narrow range of risk values, with differences between the minimum and maximum values of about 1.2 and 1.1 times, respectively.

It is important to note that this QMRA was conducted based on data from the literature (Heuvel 2019) and takes a worst-case scenario approach by considering untreated cellulose fibres. This approach results in an overestimation of the overall risk compared to a real-world scenario, as already observed. Although cellulose fibres undergo a drying process at high temperatures, it is not currently possible to quantify the reduction in pathogens due to this disinfection treatment. To improve the accuracy and specificity of the QMRA model, it would be valuable to apply it to measured data or to collect additional information on the disinfection treatments applied to all raw materials prior to their use.

4. CONCLUSIONS

The paper presents a new framework for assessing human health risks associated with the production of bio-composite materials made by recovering resources from the water cycle (e.g., calcite from drinking water treatment and cellulose from wastewater treatment). The framework consists of two steps. The first step is to identify the key health hazards using the HAZOP method. These are then used to produce a risk map linking the hazards to potential health consequences via key risk exposure mechanisms, i.e., cause–effect type events. The map is produced using the ETA qualitative risk analysis method. In the second stage of the risk assessment framework, the risk map produced in the first stage is used to quantify different aspects of human health risks. The objective here is the health risks arising from chemical and microbial contamination of raw materials and their transfer to a worker. The corresponding non-cancer risks, cancer risks, and microbial risks were assessed using the QCRA and QMRA methods, respectively. Sensitivity analysis was used to overcome the lack of some input data for the risk assessment and to assess the robustness of the results obtained.

The framework was applied to a case study where four bio-composite materials currently prototyped in the Netherlands were assessed for potential human health risks. The results obtained lead to the following conclusions:

1. The proposed framework for assessing risks to human health operates effectively. Using this framework, the primary hazards and associated risks can be identified, mapped, and then quantitatively assessed. As a result, it is possible to identify problems associated with different components of bio-composite material and to detect weaknesses in their production.
2. The toxicological aspect of human health risk was assessed using the QCRA method with adapted inputs. The overall non-cancer risk is below the safety threshold for all four materials analysed. Material M4 is representative of the worst-case due to the presence of furfuryl alcohol in the furan resin used in this material. Regarding the cancer aspect of human health risk, all four materials have a total risk value above the threshold. This is mainly caused by exposure via dermal and ingestion routes to the contaminated dust generated during the mixing of various components. However, all this can be easily addressed by asking the workers to wear masks and gloves during the production process. Furthermore, adequate safety procedures and PPE for handling resins must be applied.
3. The microbial aspect of human health risk was assessed using the QMRA method with adapted inputs. The results obtained show that *E. coli* is a pathogen of concern, based on the data used in this study for QMRA. This is a potential issue only in material M3 because of the use of cellulose fibres recovered from wastewater treatment in this material. However, this risk assessment was conducted based on a worst-case scenario assuming untreated cellulose fibres. In reality, these fibres will be treated by using a drying process at high temperature which is likely to remove *E. coli* and bring the overall risk below a safe threshold. In addition, the moulding process through the heat transfer would inactivate the remained pathogens in the dough.
4. Sensitivity analysis proves to be a valuable tool for addressing the absence of certain input data in risk assessment. The results of the sensitivity analysis indicate that the concentrations of chemicals and pathogens are the most influential input parameters, as variations in their respective concentrations produce the widest range of health risk outcomes. In scenarios s4 and s3 for QCRA and QMRA, respectively, all uncertain inputs are simulated concurrently. This approach yields a broader range of estimated risk values compared to scenario s0, where only the concentrations of chemicals and pathogens are simulated while the other input parameters remain fixed.

Future research should consider the implementation of the framework. Firstly, analysing the quality of the air in the laboratory where biocomposites are produced is crucial for better evaluating the inhalation exposure. Therefore, further research is necessary to assess the validity of this approach for other exposure routes. Additionally, the QMRA model was only performed by considering the ingestion exposure route and relied on previously researched pathogen concentrations from the literature. To improve the QMRA, it is essential to gather additional microbial data and incorporate other pathogens and exposure routes like inhalation and dermal exposure. Analysing samples collected from workers' hands would be valuable in indicating microbial exposure via hand-to-mouth route. This approach would also reinforce the developed framework, which has proven effective in assessing human health risks during the production process of a new type of bio-composite materials.

ACKNOWLEDGEMENTS

This work is part of the project WIDER UPTAKE (www.wider-uptake.eu). This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 869283. This paper reflects only the authors' view; the Commission is not responsible for any use that may be made of the information it contains.

DATA AVAILABILITY STATEMENT

All relevant data are included in the paper or its Supplementary Information.

CONFLICT OF INTEREST

The authors declare there is no conflict.

REFERENCES

Asante-Duah, K. 2017 *Public Health Risk Assessment for Human Exposure to Chemicals,* 2nd edn, Vol. 27. Springer. https://doi.org/10.1007/978-94-024-1039-6

Ashbolt, S. A. P. N. J. 2005 *WHO Guidelines for the Safe Use of Wastewater and Excreta in Agriculture Microbial Risk Assessment Section*. World Health Organization (W.H.O.), Geneva.

Carvalho, V. H. C. d. 2015 *Comparative Analysis of Bio-Composites vs Conventional Composites for Technical Parts: Technical, Economical and Environmental Performances*. Tecnico Lisboa. Available from: https://fenix.tecnico.ulisboa.pt/downloadFile/563345090414261/dissertacao.pdf

Center for Chemical Process Safety 1999 *Guidelines for Chemical Process Quantitative Risk Analysis*. Center for Chemical Process Safety of the American Institute of Chemical Engineers, New York (NY).

Dehghani, M., Rezaie Rahimi, N., Zarei, M., Parseh, I., Soleimani, H., Keshtkar, M., Zarei, A. A. & Khaksefidi, R. 2022 Chemical and radiological human health risk assessment from uranium and fluoride concentrations in tap water samples collected from Shiraz, Iran; Monte-Carlo simulation and sensitivity analysis. *International Journal of Environmental Analytical Chemistry* 1–16. https://doi.org/10.1080/03067319.2022.2038145

Delli Compagni, R., Gabrielli, M., Polesel, F., Turolla, A., Trapp, S., Vezzaro, L. & Antonelli, M. 2020 Risk assessment of contaminants of emerging concern in the context of wastewater reuse for irrigation: An integrated modelling approach. *Chemosphere* **242**, 125185. https://doi.org/10.1016/j.chemosphere.2019.125185.

Deng, Y., Bonilla, M., Ren, H. & Zhang, Y. 2018 Health risk assessment of reclaimed wastewater: A case study of a conventional water reclamation plant in Nanjing, China. *Environment International* **112**, 235–242. https://doi.org/10.1016/j.envint.2017.12.034.

E.P.A. 2022 *Human Health Risk Assessment*. EPA: United States Environmental Protection Agency. Available from: https://www.epa.gov/risk/human-health-risk-assessment

E.P.A. 2023 *Basic Information About the Integrated Risk Information System*. Available from: https://www.epa.gov/iris/basic-information-about-integrated-risk-information-system

Haugen, S. & Rausand, M., 2011 In: *Risk Assessment: HAZOP* (Marvin, R. ed.), Norwegian University of Science and Technology (NTNU), Trondheim, pp. 1–46.

Heuvel, M. F. v. d. 2019 *Analyses op Zeefgoed in het Kader van Dossiervorming Celluloseketen*. STOWA. Available from: https://edepot.wur.nl/545947

Safety data sheet according to Regulations (EC) 1907/2006. International Furan Chemicals B.V. Version 13.1 Revision 05/05/2022 URL: https://www.furan.com/products/furfuryl-alcohol/.

Johansen, A. M. 2010 Monte Carlo methods. In: *International Encyclopedia of Education,* 3rd edn, Baker, E. L., Peterson, P. L. & McGraw, B. (eds.), Elsevier Science, Burlington, pp. 296–303. https://doi.org/https://doi.org/10.1016/B978-0-08-044894-7.01543-8.

Mohanty, A. K., Misra, M. A. & Drzal, L. T. 2002 Sustainable bio-composites from renewable resources: Opportunities and challenges in the green materials world. *Journal of Polymers and the Environment.* **10**, 19–26.

Nativio, A., Kapelan, Z. & van der Hoek, J. P. 2022 Risk assessment methods for water resource recovery for the production of bio-composite materials: Literature review and future research directions. *Environmental Challenges* **9**, 100645. https://doi.org/10.1016/j.envc.2022.100645.

NJDEP 2021 *Soil Remediation Standards for the Ingestion-Dermal Exposure Pathway*. Available from: https://www.nj.gov/dep/srp/guidance/rs/bb_ingestion_dermal.pdf

OEHHA 2012 *Residential and Worker Exposure Duration, Individual vs. Population Cancer Risk, and Evaluation of Short Term Projects*. Technical Support Document for Exposure Assessment and Stochastic Analysis. Available from: https://oehha.ca.gov/media/downloads/crnr/chapter112012.pdf

Partyka, M. L. & Bond, R. F. 2022 Wastewater reuse for irrigation of produce: A review of research, regulations, and risks. *Science of the Total Environment* **828**, 154385. https://doi.org/10.1016/j.scitotenv.2022.154385.

Quantitative Microbial Risk Assessment – The quantitative microbial risk assessment framework 2017 *Highest Quality Models and Parameters*. Available from: https://qmrawiki.org/content/highest-quality-models-and-parameters?page=1

RAIS 2022a *The Risk Assessment Information System – Chemical Specific Parameters*. Available from: https://rais.ornl.gov/cgi-bin/tools/TOX_search?select=chemspef

RAIS 2022b *The Risk Assessment Information System – Chemical Toxicity Values*. Available from: https://rais.ornl.gov/cgi-bin/tools/TOX_search?select=chemtox

RAIS 2023 *The Risk Assessment Information System*. Available from: https://rais.ornl.gov/cgi-bin/tools/TOX_search?select=chemtox

Roy, S. B., Shit, D. S. C., Gupta, D. R. A. S. & Shukla, D. P. R. 2014 A review on bio-composites: Fabrication, properties and applications. *International Journal of Innovative Research in Science, Engineering and Technology* **03** (10), 16814–16824. https://doi.org/10.15680/ijirset.2014.0310058.

RSL 2020 *Regional Screening Level (RLS) Summary Table (TR = 1e-06, HQ = 1)*. Available from: https://support.esdat.net/Environmental%20Standards/us/region_3_6_9/regional%20screening%20level%20(rsl)%20summary%20table%20(tr=1e-06,%20hq=1)%20may%202020%20(corrected).pdf

Ruiken, C. J., Breuer, G., Klaversma, E., Santiago, T. & Van Loosdrecht, M. C. M. 2013 Sieving wastewater–cellulose recovery, economic and energy evaluation. *Water Research* **47** (1), 43–48. https://doi.org/10.1016/j.watres.2012.08.023.

Schetters, M. J., van der Hoek, J. P., Kramer, O. J., Kors, L. J., Palmen, L. J., Hofs, B. & Koppers, H. 2015 Circular economy in drinking water treatment: Reuse of ground pellets as seeding material in the pellet softening process. *Water Science and Technology* **71** (4), 479–486. https://doi.org/10.2166/wst.2014.494.

Selvam, S., Jesuraja, K., Roy, P. D., Venkatramanan, S., Khan, R., Shukla, S., Manimaran, D. & Muthukumar, P. 2022 Human health risk assessment of heavy metal and pathogenic contamination in surface water of the Punnakayal Estuary, South India. *Chemosphere* **298**, 134027. https://doi.org/10.1016/j.chemosphere.2022.134027.

Singh, J. & Lee, B. K. 2015 Pollution control and metal resource recovery for low grade automobile shredder residue: A mechanism, bioavailability and risk assessment. *Waste Management* **38**, 271–283. https://doi.org/10.1016/j.wasman.2015.01.035.

United Nations 2023 *The 17 Goals – Sustainable Development*. Department of Economic and Social Affairs. Available from: https://sdgs.un.org/goals

U.S.E.P.A. 1989 *Risk Assessment Guidance for Superfund – Volume I – Human Health Evaluation Manual (Part A)*. D. C. Office of Emergency and Remedial Response U.S. Environmental Protection Agency, Washington, DC.

U.S.E.P.A. 2005 *Guidelines for Carcinogen Risk Assessment*. Risk Assessment Forum – U.S. Environmental Protection Agency, Washington, DC.

U.S.E.P.A. 2009 *Risk Assessment Guidance for Superfund Volume I: Human Health Evaluation Manual (Part F, Supplemental Guidance for Inhalation Risk Assessment)*. Office of Superfund Remediation and Technology Innovation, Environmental Protection Agency, Washington, DC.

U.S.E.P.A. 2011a Chapter 5 – soil and dust ingestion. In: *Exposure Factors Handbook*. (National Center for Environmental Assessment, ed.), Office of Research and Development, U.S. Environmental Protection Agency (E.P.A.), Washington, DC

U.S.E.P.A. 2011b Chapter 6 – inhalation rates. In: *Exposure Factors Handbook*. (National Center for Environmental Assessment, ed.), Office of Research and Development, U.S. Environmental Protection Agency (E.P.A.), Washington, DC

U.S.E.P.A. 2011c Chapter 7 – dermal exposure factors. In: *Exposure Factors Handbook*. (National Center for Environmental Assessment, ed.), Office of Research and Development, U.S. Environmental Protection Agency (E.P.A.), Washington, DC

U.S.E.P.A. 2011d *Exposure Factors Handbook*. EPA/600/R-09/052F. Available from: https://www.epa.gov/expobox/about-exposure-factors-handbook#about

U.S.E.P.A. 2022 *Reference Dose (RfD): Description and Use in Health Risk Assessments*. Available from: https://www.epa.gov/iris/reference-dose-rfd-description-and-use-health-risk-assessments

U.S.E.P.A. 2023 *Risk Evaluations for Existing Chemicals Under TSCA*. Available from: https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/risk-evaluations-existing-chemicals-under-tsca

U.S.E.P.A., IRIS 2023 *Integrated Risk Information System*. EPA – United States Environmental Protection Agency. Available from: https://www.epa.gov/iris

van der Hoek, J. P., de Fooij, H. & Struker, A. 2016 Wastewater as a resource: Strategies to recover resources from Amsterdam's wastewater. *Resources, Conservation and Recycling* **113**, 53–64. https://doi.org/10.1016/j.resconrec.2016.05.012.

W.H.O. 2016 *Quantitative Microbial Risk Assessment: Application for Water Safety Management*. World Health Organization (W.H.O.), Geneva.

Zhang, H. & Weng, Y. 2021 Safety risks of plant fiber/plastic composites (PPCs) intended for food contact: A review of potential hazards and risk management measures. *Toxics* **9** (12). https://doi.org/10.3390/toxics9120343.

Zubair, M., Arshad, M. & Ullah, A. 2021 Nanocellulose: A sustainable and renewable material for water and wastewater treatment. In: *Natural Polymers-Based Green Adsorbents for Water Treatment*, pp. 93–109. https://doi.org/10.1016/b978-0-12-820541-9.00009-0.

First received 12 June 2023; accepted in revised form 12 February 2024. Available online 22 February 2024