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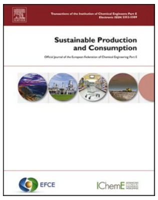

Driving sustainability at early-stage innovation in production of zinc oxide nanoparticles

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ABSTRACT

Despite its industrial relevance and the methods that have been described for its synthesis, little is known about the performance of the production processes of ZnO nanoparticles (ZnO NPs), either pure or doped, from the sustainability perspective. The Safe-and-Sustainable-by-Design (SSbD) framework brings to this context an excellent opportunity to 1) evaluate the impacts of chemical processes from the safety and sustainability perspectives, and 2) design and test safety and sustainability strategies to study and optimise these key aspects in early innovation stages. This work aims at assessing the production of ZnO NPs using this approach, testing the sustainability of the materials, designed and produced by Phornano, an Austrian SME, under this scheme. Three scenarios were analysed: the original process (BS) and two alternatives resulting from the application of SSbD strategies to the former (S1 and S2). BS is a linear process in which $Zn(NO_3)_2{\cdot}6H_2O$, whey, water and a dopant (a Mn salt) are used as starting materials. However, obtention of the desired product entails the release of toxic fumes (SO_x and NO_x) to the atmosphere. S1 and its scale-up version, S2, are circular processes in which SO_x emissions are avoided, due to the replacement of whey by a non-aminated starch, and NO_x are transformed into HNO_3, which reacts with Zn powder to produce $Zn(NO_3)_2{\cdot}6H_2O$; in this way, no harmful substances are freed and the zinc salt employed as a raw material in BS is generated during the manufacture of ZnO NPs. Four well-known evaluation tools were employed to achieve a holistic sustainability perspective: Environmental Life Cycle Assessment (LCA), Material Flow Cost Accounting (MFCA), Social Life Cycle Assessment (S-LCA) and Multi-Criteria Decision Analysis (MCDA), according to the standardised methodologies or the most broadly spread ones; the study was complemented with an uncertainty analysis. The results for the production of 1 kg of ZnO NPs show that the after-SSbD scenarios are remarkably more sustainable than BS: the environmental evaluation reveals that S2 outperforms BS for 10 environmental indicators, allowing a reduction of 67 % in terms of total aggregated impact (from 13.7 to 4.4 mPt); from the economic viewpoint, synthesis of ZnO NPs through S2 is around four times cheaper than that achieved *via* BS (512 *vs* 2206 €); finally, the social footprint is reduced from 159 mPt in the original process to 21 mPt in S2. MCDA of BS, S1 and S2 considering the three assessments performed confirms that S2 is, with almost 100 % probability, the best-performing alternative from the sustainability perspective, followed by S1. Overall, this work, the most complete in this field to date, contributes to

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the sustainable synthesis of ZnO NPs and to the methodological advance of the SSbD framework through the revision of its limitations and opportunities.

1. Introduction

Nanomaterials (NMs) are appealing because of their high stability, straightforward synthetic methods and easy control over aspects like size and shape (Negrescu et al., 2022). Among these materials, ZnO is the most widely used, since its chemical and optical properties can be easily tuned (Mandal et al., 2022). This work focuses on improving the sustainable synthesis of this compound, combining functionality with reduced environmental, economic and social impacts. ZnO exhibits excellent thermal and chemical stabilities (Skorenko et al., 2016; Heinonen et al., 2017), it is biocompatible (Stefanidou et al., 2006) and biodegradable (Kielbik et al., 2017), and the raw materials required for its production are accessible (El Faroudi et al., 2023). These advantages have turned ZnO nanoparticles (NPs) into a valuable multifunctional material, key to the development of Green Technologies (Klingshirn et al., 2010), that has been employed, for instance, in sunscreens (Schneider and Lim, 2019) and biomedical imaging (Hahm, 2014). These are the two main applications of the ZnO NPs manufactured by PHORNANO Holding GmbH (hereafter Phornano), the company that has produced ZnO NPs according to the processes described in this work. Several physical, chemical and biological methods have been reported for the synthesis of nanoscale materials altogether, and of ZnO NPs in particular (Mekuye and Abera, 2023); some of them are shown in Fig. 1. In this work, ZnO NPs were prepared through a hybrid strategy: a sol-gel method assisted by whey, a by-product of the production of cheese or casein (Soares et al., 2020), or by a non-aminated starch, a polysaccharide (Nain et al., 2020).

Although ZnO NPs have been extensively studied, the potential of sustainable hybrid synthetic methodologies, particularly those incorporating renewable by-products, such as whey or starch, remains significantly underexplored. These approaches pose a promising avenue by utilising abundant, cost-effective and biodegradable resources, thereby aligning with the principles of sustainability and circular economy (United Nations, 1987). This research gap highlights the urgent necessity of developing environmentally sustainable synthetic strategies for the tailored functionalisation of ZnO NPs. In this context, this work aims at assessing and comparing the sustainability of the production of ZnO NPs before and after applying the Safe-and-Sustainable-by-Design (SSbD) framework (European Commission, 2022), implementing the identified safety and sustainability recommendations. Use of this framework, which is a general approach to steer innovation towards safe and sustainable materials (in this case, NMs) (Pizzol et al., 2023) throughout their life cycles (Furxhi et al., 2023; Caldeira et al., 2024), has allowed to pinpoint key sustainability hotspots and to evaluate the effectiveness of the proposed redesign measures to mitigate those impacts. The SSbD methodology consists of five steps, Steps 1, 2 and 3, associated to safety, and Steps 4 and 5, related to environmental and socio-economic analyses, respectively. Safe-by-Material (SbMD) and Safe-by-Process (SbPD) approaches, two particular sets of SSbD strategies, were applied to improve Phornano's original production process (BS), leading to definition of two new scenarios, S1 and S2, that are described below; both SbMD and SbPD are part of the background research of this work, which is focused on Steps 4 and 5. Although the European Commission recommends the early application of SSbD in the innovation process (Abbate et al., 2024), challenges have been identified in various case studies (Caldeira et al., 2023), as well as difficulties experienced by companies when trying to implement SSbD (European Environment Agency, 2020; CEFIC, 2021, 2022; ChemSec, 2021). For instance, the homogenised terminology and SSbD criteria, evaluation tools, data availability and quality, methods for scaling up laboratory data to an industrial level, and others (Abbate et al., 2025). Within Steps 4 and 5, data availability, quality and uncertainty, and tools, are the main concerns (Caldeira et al., 2022; Abbate et al., 2025); besides, a holistic view of the application of the SSbD framework has been highlighted as a desirable approach to connect all value chain stakeholders and facilitate co-creation of SSbD solutions (Soeteman-Hernández et al., 2024; Abbate et al., 2025). As Step 5 is an optional step of the framework and, differently from Step 4, there are not universally accepted methodologies to conduct the socio-economic evaluation, this work intends to assess the usefulness of the selected social and economic tools, and delve into data and uncertainty analysis for BS, S1 and S2 from the three sustainability pillars viewpoint, considering also the integration of the results through a Multi-Criteria Decision Analysis (MCDA) tool (Prado and Heijungs, 2018; Tschulkow, 2024), which allows for balancing complex trade-offs among environmental, social and economic factors. Altogether, this work contributes to filling some of the gaps found in the application of Steps 4 and 5 of the framework, and to the global analysis of the results of LCA, MFCA and S-LCA studies.

As indicated in *Section 2*, sustainability studies about NMs

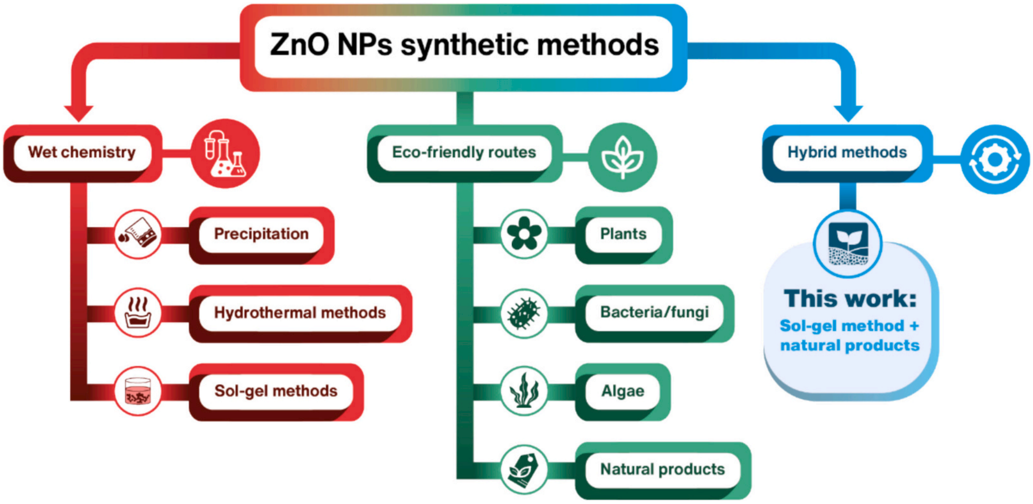

Fig. 1. Some of the methods described in the literature for the synthesis of ZnO NPs: wet chemistry, eco-friendly routes and hybrid methods.

manufacturing processes in general, and of ZnO NPs in particular, are limited, which means a research gap in the identification of critical environmental, economic and social hotspots within those processes, and application of correcting measures to reduce the corresponding impacts, particularly according to the SSbD approach. Analysing the influence of uncertainties on the final results is also key, especially for low-TRL processes like those described here. This work aims at covering this gap by studying and comparing the hotspots of BS, S1 and S2, and the uncertainties of the final results, considering the three sustainability pillars and integration of results through the methods described in *Section 3*. The three scenarios are represented in Fig. 2. Briefly (for a more detailed discussion, see *Section 3.1*), BS is the initial alternative, in which $Zn(NO_3)_2{\cdot}6H_2O$, a Mn salt, whey and water are used as raw materials to ultimately yield the ZnO NPs, but with the concomitant formation of toxic fumes (SO_x and NO_x). S1 and S2, the latter being an adapted and upscaled scenario with respect to S1, avoid such emissions by replacing whey by starch (SO_x), and by returning NO_x to the system to produce useful reagents (HNO_3) that eventually react with Zn powder to generate $Zn(NO_3)_2{\cdot}6H_2O$, and from here the desired good.

This study not only advances sustainable nanotechnology by optimising the synthesis of ZnO NPs for various applications but also provides practical guidance on the operationalisation of the socio-economic integration aspects of the SSbD approach. In particular, it contributes to the holistic sustainability evaluation, considering environmental, economic and social results. The findings of this research highlight its potential to support safety and sustainability in industrial processes from the earliest stages of innovation. By demonstrating the feasibility of hybrid green methods and the application of the SSbD approach to their study and improvement, this work lays a foundation for safer, more sustainable nanotechnology innovations, with results that are useful not only for academia but also for stakeholders and contribute to the development of these studies for NMs-based low-TRL technologies.

2. Literature review

The blooming of nanotechnology and the ubiquity of NMs, such as the discussed ZnO, have encouraged the eco-friendly design and the sustainable use of these goods (Hutchison, 2016; Pokrajac et al., 2021; Chausali et al., 2023). Simultaneously, concerns about the sustainability of the production processes of NMs, including NPs emissions to the environment, have been raised (Buist et al., 2017; Salieri et al., 2019; Martínez et al., 2021; Arora et al., 2024). Among different evaluation tools, Life Cycle Assessment (LCA) has been commonly employed to quantify the impacts associated to the life cycle of a product. For an emerging technology such as NMs that often only functions at a lab or pilot scale, ex-ante LCA has become an essential instrument for identifying potential hotspots and guiding sustainable design (Cucurachi et al., 2018; Cucurachi and Blanco, 2022). For instance, Tan et al. (2018) performed an ex-ante LCA for cellulose nanocrystal foam along the R&D trajectory, describing the design improvements. Pallas et al. (2020) conducted an ex-ante LCA study of the emerging gallium-arsenide nanowire and provided a benchmark for the commercialisation of the technology. Recently, a framework for ex-ante LCA of nano-reinforced biopolymers at low TRL (Technology Readiness Level) was proposed and applied, and the environmental hotspots identified (Müller-Carneiro et al., 2023). However, the use of Life Cycle Assessment (LCA) (and, particularly, ex-ante LCA) as a tool to quantify the environmental footprint of the manufacturing of these materials (Meyer and Upadhyayula, 2014) is still at an early stage (Hachhach et al., 2022). According to a recent review, from 2001 to 2020 only 71 studies revolving around LCA of NMs were published (Nizam et al., 2021). Techno-economic analyses of NMs production processes, in some cases complemented with LCA studies, have also been reported (de Assis et al., 2018; Ragadhita et al., 2019; Karadaghi et al., 2023; Rajendran et al., 2023), but S-LCA investigations in this context are scarce (Handy and Shaw, 2007; Stoycheva et al., 2022). Multi-objective problem-solving strategies are highly recommended to achieve a meaningful interpretation of results (Jia et al., 2016), since these approaches allow to simultaneously analyse and balance conflicting goals (*e.g.*, reducing environmental impacts *vs* minimising operational costs); the holistic nature of the assessment and the consideration of uncertainties also permits to reduce bias, thus improving confidence in the outcome. Multi-Criteria Decision Analysis (MCDA) (Cinelli et al., 2017) is one of the tools used for this purpose; it is a valuable methodology to analyse several scenarios (as BS, S1 and S2; see *Section 1*) and various indicators (*e.g.*, environmental, economic and social) at the same time. However, concerning NMs the use of MCDA is not as common as would be expected. Indeed, despite the comprehensive outcomes they provide, the former methodologies still raise challenges for their application to NPs, *e.g.*, the complex modelling of the consequences of NPs release (Hischier et al., 2017) and the uncertain modelling of low-TRL technologies. In the case of ZnO NPs, to the best of our knowledge there is only one published LCA study, which addresses the microwave-assisted synthesis of this material, although not from a circular perspective (Papadaki et al., 2017). Few techno-economic assessments dealing with the production of this NM have been reported (Zahra et al., 2020; Yashni et al., 2021). Neither S-LCA nor MCDA studies have been found in the literature. The inclusion of S-LCA and MCDA in this work is therefore a progress beyond state of the art.

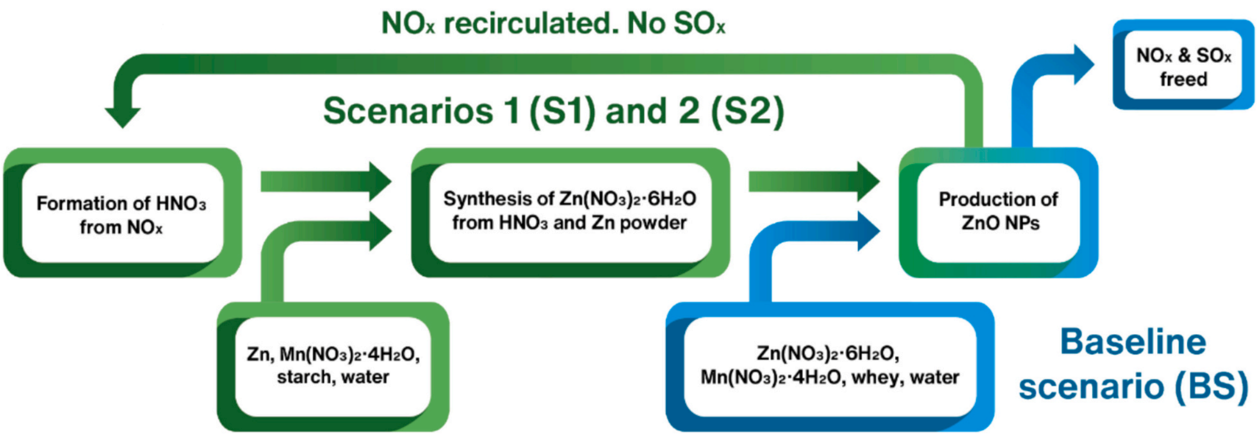

Fig. 2. Simplified diagram of the manufacturing process of ZnO NPs through the baseline scenario (BS, highlighted in blue) and scenarios 1 and 2 (S1 and S2, respectively, highlighted in green; S2 is an adapted and upscaled version of S1). The last step (production of ZnO NPs) is shown as a green-blue gradient since it is a common step for the three processes.

3. Methods

In order to perform the present investigation, four assessment tools were employed: LCA, MFCA, S-LCA and MCDA. LCA is a standardised methodology aiming at evaluating the environmental impacts of products, processes or services throughout their life cycle, according to ISO 14040 (2006) and 14044 (2006); this is the recommended approach within the SSbD framework. MFCA is standardised through ISO 14051 (2011); it focuses on material and energy flows to pinpoint and quantify waste and losses of production processes in monetary terms (Bierer et al., 2015). Differently from traditional costing methods, MFCA highlights not just the direct costs of undesirable outputs (in terms of lost sale revenue), but also all the upstream value loss in cost drivers like labour, raw materials and invested capital, that are also wasted (Schmidt, 2015). Thus, it is a useful tool not only in terms of cost accounting, but also in promoting improvements in resource efficiency and consequent reduction in environmental impact. The third tool, S-LCA, the least developed of this group, follows a similar approach to that of LCA, its purpose being to identify, prioritise and evaluate all the social impacts derived from the life of the object of study. Although there is not a universally accepted methodology to conduct S-LCA, the guidelines developed by UNEP/SETAC are the most widely spread attempt (Benoît Norris et al., 2020; Traverso et al., 2021). According to these guidelines, a Reference Scale Approach (RSA) was followed for the assessment through a database-assisted S-LCA. This method proposes to analyse the social performance opposite international and sectorial standards and statistics, which allows navigating uncertainties of low-TRL processes through a screening of potential hotspots. Finally, MCDA is a decision-supporting method that addresses intricate problems with high uncertainties and considers mutual differences. This tool allows to integrate two or more scenarios (*e.g.,* the production of ZnO nanopowder by three alternatives; *vide infra*) and two or more indicators (for instance, environmental, economic and social indicators) in a comparative study to decide which one is the best-performing process from a particular perspective (for example, sustainability). To perform this analysis, the Excel worksheet developed by Tschulkow (2024), based on the work by Prado and Heijungs (2018), was employed.

3.1. Case study

This study was performed to evaluate the environmental, economic and social impacts derived from the production of doped ZnO NPs by Phornano, an Austrian SME (small and medium-sized enterprises) focused on the research, development and manufacturing of functional NMs. The manufactured Mn-doped ZnO NPs are used as a raw material for: (a) formulations leading to the development of sunscreens, as ZnO strongly absorbs UVA and UVB radiations (Antoniou et al., 2008), and (b) fluorescent nanoprobes for biomedical imaging, as replacement for the less safe Cd-based quantum dots (see *Section 1*) (Hahm, 2014). Initially, a process leading to the annual production of 2.5 kg of doped ZnO nanopowder (the baseline scenario, BS) was performed. By employing the Safe-and-Sustainable-by-Design (SSbD) methodology, key process inefficiencies were identified, and evidence-based recommendations provided to optimise performance, safety and global sustainability. Implementation of such recommendations resulted in two redesigned scenarios, S1 and S2, which were systematically re-evaluated to quantify their impact and validate the robustness of the proposed approach. Comprehensive physicochemical characterisation, integrated with toxicokinetic modelling, demonstrated that the reengineered materials and processes exhibited equivalent or superior functional properties compared to those of the original material (BS). The results of the sustainability studies conducted for the three processes are analysed in this work. The three alternatives were developed by Phornano within the framework of the ‘Diagonal’ European research project (GA 953152). The synthesis of doped ZnO NPs according to BS starts with the dissolution of zinc nitrate hexahydrate ($Zn(NO_3)_2{\cdot}6H_2O$) and manganese(II) nitrate tetrahydrate ($Mn(NO_3)_2{\cdot}4H_2O$) in water under stirring and heating at 90 °C. This is followed by the insertion of a gelling agent; initially, whey was used as a chelating species (BS), but afterwards it was replaced by a non-aminated starch, a vegan alternative (*i.e.*, free of animal sources or processing aids derived from animals, or animal by-products) to whey (S1 and S2). Both whey and starch avoid the use of citric acid and ethylene glycol, other commonly employed reagents in this process (Soares et al., 2020). Polymerisation takes place after the insertion of the chelating agent, driving to the formation of a gel that is heated in a drying oven for one hour at 200 °C to remove the water excess. A nanofoam is obtained and subsequently calcinated (400 °C), leading to the desired ZnO nanopowder. In the case of S1 and S2, the gel is treated in a closed reactor, thus avoiding the release of nitrogen oxides (NO_x), which flow into a water bath to turn them into nitric acid (HNO_3), that ultimately reacts with Zn powder to produce $Zn(NO_3)_2{\cdot}6H_2O$, restarting the cycle. In both scenarios the calcination step is circumvented, with the consequent energy saving (*vide infra*, and see also Figs. 3 and 4).

After carrying out the physicochemical, toxicological and sustainability evaluations of BS, a set of Safe-by-Material and Safe-by-Process design alternatives (SbMD and SbPD, respectively) were identified and applied. Regarding SbMD, doping of ZnO with Mn was performed. As the VERDEQUANT process (Stingl et al., 2021; Phornano, 2024) supports doping of ZnO quite well (Picasso et al., 2022; Assis et al., 2024), samples were produced *via* this method. Concerning SbPD, three improvements were applied:

- Creation of a NOFLOW box to enhance the safety of the handling process. The NOFLOW box is a workplace shielded against airflow and with a screen to protect the operator. Its design is similar to that of a flowbox, but without any ventilation to avoid nanopowders to be blown away during handling and filling.
- Conversion of NO_x into HNO_3, thus allowing the circularity of the above-mentioned VERDEQUANT manufacturing process.
- Substitution of whey by a non-aminated starch, a vegan formulation, thus avoiding the formation and release of sulfur oxides (SO_x), an unwanted by-product.

These modifications in the production process led to the definition of two new scenarios:

- Scenario 1 (S1): application of the above-mentioned SbMD and SbPD strategies to a small amount of product (2.5 kg).
- Scenario 2 (S2): application of those strategies to a larger-scale scenario, leading to 100 kg of produced doped ZnO NPs.

The linearity of BS and the circularity of S1 and S2 are explained in Fig. 3. S2 differs from S1 mainly in two aspects: on the one hand, in S1 both $Zn(NO_3)_2{\cdot}6H_2O$ and Zn powder are employed as raw materials, whereas in S2 only Zn powder is used. On the other, S2 is an upscaled scenario: 100 kg of doped ZnO NPs are manufactured *via* this process, and 2.5 kg are obtained through S1. In S2, a larger reactor, with a higher energy efficiency, is employed. The selected functional unit (FU), as explained in the next section, is identical for the three studied processes, to allow for a proper comparison.

Once the LCA, MFCA and S-LCA results for S1 and S2 were analysed, they were subjected, together with those of BS, to a Multi-Criteria Decision Analysis (MCDA) to determine which of the three approaches was the best-performing process from the sustainability point of view.

3.2. Goal and scope

As indicated in *Section 3.1*, the main objective of this work is to study the environmental, economic and social performance and, altogether, the sustainability of the production process of doped ZnO NPs according to the experimental procedure conceived by Phornano, and to compare

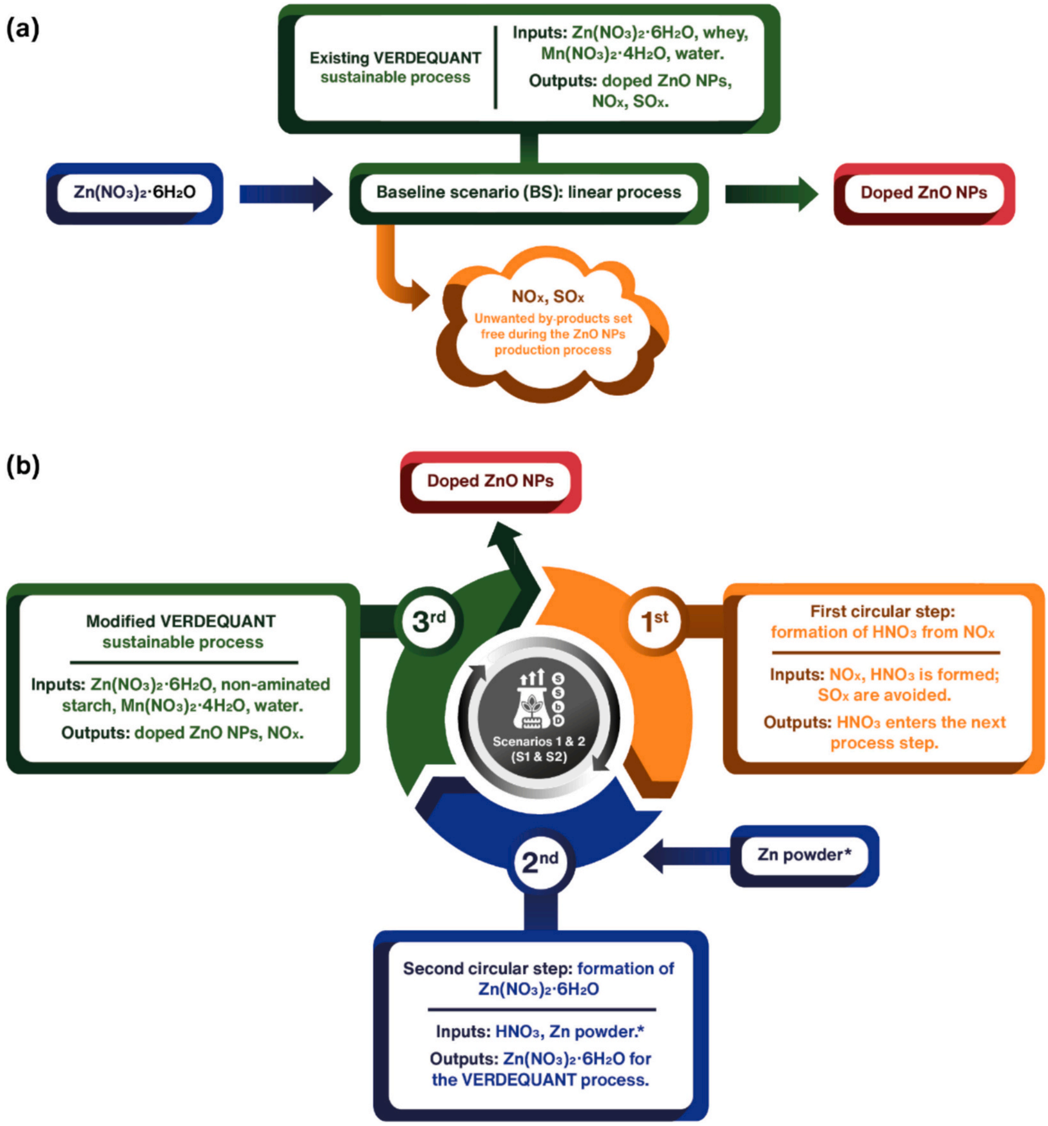

Fig. 3. Schematic representation of the production process of ZnO NPs through BS (a), and S1 and S2 (b). In the case of S1 and S2, the generated NO_x are transformed into HNO_3, which reacts with Zn powder to produce $Zn(NO_3)_2·6H_2O$; in BS, the last reagent enters the process as such. After adding $Mn(NO_3)_2·4H_2O$, the insertion of whey (BS) or a non-aminated starch (S1 and S2) takes place. Following a suitable treatment (*Section 3.1*), Mn-doped ZnO NPs are obtained, with the concomitant formation of NO_x that enter the cycle again (S1 and S2). This design allows recirculating NO_x and avoids the emission of SO_x (BS). *In S1 a mixture of $Zn(NO_3)_2·6H_2O$ and Zn is employed.

this process with two scenarios resulting from the application of SSbD strategies to the former in an integrating study. Environmental, economic and societal arguments, analysed both separately and combined, are provided to select the most advisable alternative from the sustainability perspective. This, together with the life cycle inventory datasets included in this work, will contribute to the state-of-the-art knowledge of the sustainable synthesis of nanosized ZnO for the eventual production of solar lotions (Chauhan et al., 2022) and of medical-oriented materials (Weng et al., 2023), among other applications (Raha and Ahmaruzzaman, 2022; Sharma et al., 2022).

The three scenarios were modelled consistently. Thus, the FU for BS, S1 and S2 is identical, so that the results can be compared: the production of 1 kg of ZnO nanopowder that is to be used in sunscreen formulations to achieve 50 SPF (Sun Protection Factor), at minimum 20 % concentration of the photoprotective agent (ZnO). This FU was also selected to carry out the three assessments described in this article (LCA, MFCA and S-LCA) and, consequently, MCDA. The system boundaries are also identical for the three scenarios and assessments. The present work is a 'cradle-to-gate' study that starts with the raw materials extraction and finishes with the obtention of the product of interest (Fig. 4). It should be noted that only the inputs (*e.g.*, raw materials, electricity consumption) and outputs (*e.g.*, emissions, generated waste) were collected and included within the system boundaries. Upstream activities, such as extraction or transport, were obtained from the selected database (ecoinvent v3.10, 2024), which gathers and integrates average data for each input of the production process, or from the literature, whereas downstream activities (*e.g.*, distribution, final use) were not considered in this work.

3.3. Environmental Life Cycle Assessment (LCA)

3.3.1. Life Cycle Inventory (LCI)

Table 1 displays the data of raw materials, energy and emissions, among other items, involved in the synthesis of 2.5 or 100 kg of doped ZnO NPs according to the baseline and after-SSbD scenarios (data refer to the whole production process, without differentiating individual steps). The operational inventories were normalised to the production of 1 kg of doped ZnO NPs (reference flow); all of them can be found in the

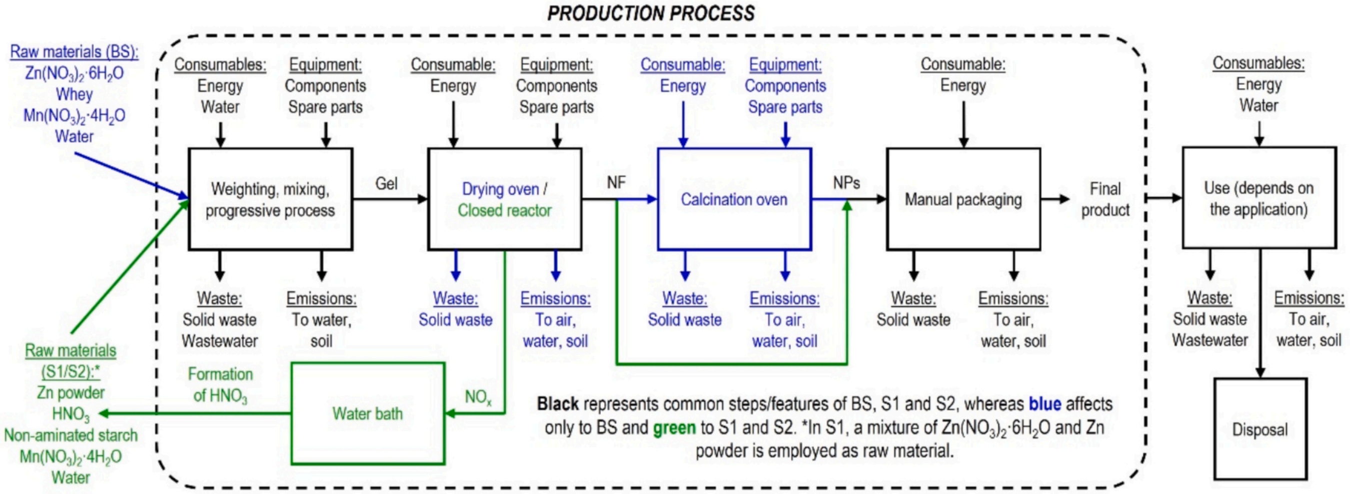

Fig. 4. Schematic view of the production process of Mn-doped ZnO nanopowder designed by Phornano through the three studied scenarios (BS, S1, S2). 'NF' stands for 'nanofoam'.

Table 1
Operational inventory data of the baseline and after-SSbD scenarios (BS: baseline scenario; S1: scenario 1; S2: scenario 2) provided by Phornano for the annual production of 2.5 (BS and S1) and 100 (S2) kg of doped ZnO nanopowder, using 1 kg of doped ZnO as the reference flow.

Flow	Unit	Normalised value			Transport distance (km)		
		BS	*S1*	*S2*	*BS*	*S1*	*S2*
Inputs							
$Zn(NO_3)_2·6H_2O$	kg	4	1.8	–	700	700	–
Zn powder (99.9 %)	kg	–	0.31	0.62	–	700	700
Non-aminated starch	kg	–	0.3	0.2	–	–	–
Whey	L	16	–	–	20	–	–
$Mn(NO_3)_2·4H_2O$	kg	0.4	0.4	0.1	700	700	700
HNO_3 (68 %)	L	–	3	3	–	–	–
Electricity from the grid, low voltage (for ZnO)	kWh	4	12	9	–	–	–
Cleaning water (tap)	L	40	40	10	–	–	–
Process water (deionised)	L	10	10	10	–	–	–
Outputs							
ZnO	**kg**	**1**	**1**	**1**	–	–	–
Wastewater from cleaning	L	50	40	10	–	–	–
NO_2 to air	kg	1.12	0.55	0.37	–	–	–

'LCI_Modelling' worksheet of the SI.

3.3.2. *Approximations, assumptions and limitations*

It was assumed that the losses of cleaning and process water are negligible (0 % losses applied) and, in order to model the transport (expressed in tons-kilometer, t·km) and production (mass unit used as reference for the ecoinvent v3.10 dataset) of whey, a density of 1 kg/L was supposed. Datasets from ecoinvent v3.10, a common LCI database, were chosen as much as representative in terms of technology (same materials and processes), geography (Austrian data if available, European or global data if not) and time (most recent data); geographical representativeness is indicated in brackets in the dataset name (AT for Austria, RER for Europe and GLO for the world). When the production processes and transport distances were known, materials were modelled with the so-called 'production' datasets (mentioned at the end of the dataset name); otherwise, 'market' datasets, which reflect the average production mix and transport means for the considered geographical area, were applied. In the case of $Zn(NO_3)_2·6H_2O$ and $Mn(NO_3)_2·4H_2O$ no background data could be found in ecoinvent v3.10 datasets. Therefore, a stoichiometric balance, coming from the reaction of ZnO and MnO, respectively, with HNO_3, was employed to model these chemicals ($MO + 2HNO_3 \rightarrow M(NO_3)_2 + H_2O$; M = Zn or Mn). All of this is reflected in Table 2.

3.3.3. *Life Cycle Impact Assessment (LCIA)*

This phase allows transforming the data collected in the previous step into environmental impacts. The Environmental Footprint (EF, v3.1) method, based on the Environmental Footprint (EF) initiative, launched by the European Commission (2013) to create a harmonised EU methodology to communicate environmental performance of products and organisations, was selected as the LCIA method since this work was developed in the European Union under the shelter of a European-Commission funded research project. This method consists of 16 midpoint impact categories (Fazio et al., 2018). As this article addresses the study of a low-TRL technology, there are no objective criteria to exclude any of the EF 3.1 indicators from the analysis and, therefore, the information provided by the 16 impact categories was deemed relevant for the work. Finally, creation of the models for the impact assessment calculation was conducted with SimaPro® 9.6 (2024) by PRé Consultants. SimaPro®, being an internationally recognised software to perform LCA studies, is used both by industry and academia, integrates

Table 2
LCI background data for the baseline and after-SSbD scenarios, obtained from ecoinvent datasets.

Flow	Background process
$Zn(NO_3)_2·6H_2O$	0.27 kg/kg 'Zinc oxide {GLO}| market for' + 0.42 kg/kg 'Nitric acid, without water, in 50 % solution state {RER w/o RU} | market for' + 0.36 kg/kg 'Tap water {Europe without Switzerland} | market for'
Zn powder (99.9 %)	'Zinc oxide {GLO}| market for'
Non-aminated starch	'Starch, from maize {GLO}| market for'
Whey	'Whey {GLO}| cheese production, soft, from cow milk'
$Mn(NO_3)_2·4H_2O$	0.40 kg/kg 'Manganese(III) oxide {GLO}| market for' + 0.70 kg/kg 'Nitric acid, without water, in 50 % solution state {RER w/o RU} | market for'
HNO_3 (68 %)	'Nitric acid, without water, in 50 % solution state {RER w/o RU}| market for nitric acid, without water, in 50 % solution state | Cut-off, U'
Electricity	'Electricity, low voltage {AT}| market for'
Water (process or for cleaning)	'Tap water {Europe without Switzerland}| market for'
Wastewater from cleaning	'Wastewater, average {Europe without Switzerland}| market for'
Lorry transport	'Transport, freight, lorry, unspecified {RER}| market for'

the above-mentioned ecoinvent database and EF method and allows to model and analyse complex scenarios, rendering key information for process optimisation, hotspots identification and sustainability improvement, thus facilitating decision-making. The EF single score (in mPt) (using the latest normalisation and weighting factors from EF 3.1) is computed as well to be used for the MCDA.

The impacts of the reported new materials/processes were assumed to not significantly disturb the economy, so they were modelled following an attributional approach, where the impacts or flows from other sectors are allocated without considering a potential change in their operations. In addition, impacts due to waste treatment were assigned to the waste producer. If such waste had an economic value, those impacts were attributed to the future user. The cut-off approach was selected to be consistent with the stated modelling choices. Impacts from infrastructures were excluded from the assessment, since they generally have a low contribution to industrial processes and are subjected to large uncertainties. Environmental flows were classified and characterised depending on their effects, and for each flow the impact was the result of multiplying the mass of a given input/output by the associated characterisation factor (*CF*) (the impacts attributable to ZnO NPs emissions were not considered at this stage since CFs are not available, a matter that is currently under study in our laboratories).

3.4. Material Flow Cost Accounting (MFCA) analysis

3.4.1. Operational cost inventory and modelling

In this *paper*, an MFCA analysis for both the baseline alternative and the after-SSbD scenarios (S1 and S2) was conducted, using the same system boundaries (Fig. 4), functional unit (1 kg of ZnO nanopowder) and mass and energy flows considered in the LCA.

This methodology offers detailed cost insights into material and energy inefficiencies during manufacturing, and provides a robust framework aligned with the goals of sustainable production (Hunkeler et al., 2008). In addition, its certification under ISO 14051 (2011) allows to enhance the transparency, reproducibility and comparability of the results. According to MFCA, the production process is divided into Quantity Centres (QC), where input materials are compared with the products to judge material losses (material loss = input – products). Since the available data were aggregated for the whole production process, a single QC was defined, reporting the complete production process of the doped ZnO NPs from start to finish. Next, all costs associated with the entry and exit of material flows for the QC are assessed and attributed to those flows, in line with the Asian Productivity Organization (Tachikawa, 2014) and ISO 14051 (2011). In MFCA, these costs are broken down into four categories (materials, energy, system and waste management) (Tachikawa, 2014).

In addition to the LCI of Table 1, inputs of equipment costs,

Table 3

Aggregated cost inventory data of the baseline and after-SSbD scenarios (BS: baseline scenario; S1: scenario 1; S2: scenario 2) provided by Phornano for the annual production of 2.5 (BS and S1) and 100 (S2) kg of doped ZnO nanopowder, using 1 kg of doped ZnO as the reference flow.

Inputs	Unit	Unit cost (€/unit)			Annual cost (€/year)		
		BS	*S1*	*S2*	*BS*	*S1*	*S2*
Raw materials							
$Zn(NO_3)_2·6H_2O$	kg	37.00	13.21	–	370.00	59.45	–
Zn powder (99.9 %)	kg	–	16.80	14.43	–	13.04	899.00
Non-aminated starch	kg	–	5.00	5.00	–	10.00	100.00
Whey	L	3.50	–	–	140.00	–	–
$Mn(NO_3)_2·4H_2O$	kg	100.00	100.00	100.00	100.00	100.00	1000.00
HNO_3 (68 %)	L	–	21.20	20	–	106.00	4000.00
Cleaning water (tap)	L	0.0010	0.0010	0.0010	0.10	0.10	1.00
Process water (deionised)	L	1.00	1.00	1.00	25.00	25.00	1000.00
Wide mouth bottles	piece	5.00	5.00	5.00	500.00	250.00	1000.00
Shipping costs	–	–	–	–	68.40	107.19	255.00
Energy							
Electricity from the grid, low voltage	kWh	0.50	0.32	0.32	10.00	9.60	288.00

Equipment

Inputs	Purchase cost (€)			Annual depreciation (%)			Annual cost (€/year)		
	BS	*S1*	*S2*	*BS*	*S1*	*S2*	*BS*	*S1*	*S2*
Magnetic stirrer	400.00	400.00	1200.00	20	20	20	80.00	80.00	240.00
Reactor	300.00	300.00	10,000.00	20	20	20	60.00	60.00	2000.00
Muffle furnace	800.00	–	–	20	–	–	160.00	–	–

Maintenance

Inputs	Frequency	Unit cost (€/unit)			Annual cost (€/year)		
		BS	*S1*	*S2*	*BS*	*S1*	*S2*
Equipment calibration	Annual	400.00	400.00	400.00	400.00	400.00	400.00

Labour

Type	Unit	Unit cost (€/unit)			Annual cost (€/year)		
		BS	*S1*	*S2*	*BS*	*S1*	*S2*
In-house labour cost	€/hour	36.00	40.00	40.00	3600.00	4000.00	40,000.00

maintenance tasks, labour expenses and shipping fees for the raw materials were considered. Output flows that have no potential economic value and are free of handling and disposal charges were disregarded, as they bear no effect on the cost results. Table 3 presents a compilation of the cost inventory. All costs are before taxes. The temporal system boundaries for this study refer to the period between 2022 and 2024 and are based on primary data from Phornano for raw materials, energy and labour. No future projections were included in the base case, as the focus was on analysing present-day production costs within the defined system boundaries. Future studies could expand the temporal boundaries to include projected costs for longer-term scenarios, incorporating factors such as technological advancements and market dynamics.

3.4.2. Approximations, assumptions and limitations

In terms of equipment allocation, the listed machinery was assigned in full to the annual production amounts of the doped ZnO nanopowder. Also, the output wastewater was only assigned with its respective raw materials expenses, while the doped ZnO NPs wasted in the cleaning and packing processes were allocated with all the upstream cost inputs necessary for the doped ZnO NPs production.

3.5. Social Life Cycle Assessment (S-LCA)

The social evaluation of the three scenarios aimed at the production of doped ZnO nanopowder involves two types of data: price information for the quantitative assessment, conducted with SimaPro® 9.6 (2024), and qualitative data, for other indicators proposed by UNEP/SETAC in its methodological sheets (Traverso et al., 2021), which were used to evaluate the risks of potential impacts and to design pathways for improvement.

The selected functional unit for the three scenarios (1 kg of doped ZnO NPs) was translated into monetary terms, and the considered activity variable was 'worker hours', which represents the intensity of work required by each country-specific sector directly related to production (Benoît Norris et al., 2018).

The Social Hotspots Database (SHDB) was used for background information and to identify and assess potential upstream impacts (Benoît Norris et al., 2018). SHDB, being one of the most widely used databases, provides information on social risks and opportunities by country and sector, and on the composition and location of the supply chain, through a Global Input-Output Model (GTAP) (Benoît Norris et al., 2018). Only 5 of the 6 categories (labour rights and decent work, health and safety, society, governance and community) about which the database provides information were considered in this study, since the sixth one (socio-economic contributions), being measured in economic terms and not in worker hours, could overlap with the MFCA analysis.

3.5.1. Social Life Cycle Inventory (S-LCI) and modelling

To build the S-LCA inventory, both background and foreground data were employed. The former are the country-sector data coming from the database. In the case of the latter, information was gathered through a questionnaire including LCA, MFCA and S-LCA information. Quantitative information on the costs and sources of each system input was collected and, to perform the S-LCA, the reference flow considered for the three processes was the production of 1 kg of doped ZnO nanopowder, expressed in monetary terms; data from the MFCA assessment was employed for normalisation. Table 4 displays the cost of the inputs of the three scenarios, classified according to their industry and country of origin.

To include the company performance, *ad hoc* worker hours for the 'Labour' input were designed, following the formulae by Smith (2019) (Eqs. 1 and 2):

$$Unit\,labour\,cost = \frac{Mean\,hourly\,salary\,for\,the\,country - sector\,(per\,employee)}{Gross\,annual\,output\,of\,the\,sector\,in\,the\,country} \tag{1}$$

$$Worker\ hours = \frac{Unit\ labour\ cost}{Mean\ hourly\ labour\ cost\ per\ employee} \tag{2}$$

By employing these newly created company-specific worker hours and deleting the database original ones, generic for the Austrian chemical industry and the macroeconomic trade network connecting this industry to the rest of the world, the uncertainty pertaining to the use of generic data was eliminated. As, while the possibility of risks occurring in the sector remained, the use of audited first-handed data about labour conditions reduced the chances of these risks occurring in the company, which is reflected on the worker hours associated to this input.

Concerning the specific worker hours calculus, an average hourly salary of 36 € per employee was considered, as stated in the inventory data provided by Phornano. According to the Austrian input-output tables for 2016 (Statistics Austria, 2020), the annual output of the *Forschungs und Entwicklungs* (Research and Development) sector was of 14,677,911 €, whereas the mean Technology and Development base salary in Austria amounted to 73,529 € per year. Phornano worker hours were calculated according to Eq. (2), throwing a result of 1.39×10^{-7} worker hours ('Phornano tailor-made worker hours' industry in Table 5). Table 5 shows the worker hours used from the database for each input's country-specific sector.

The 'Reference Scale' method (also known as S-LCA Type I method) was selected to carry out the impact assessment of the three scenarios considered in this work. Such evaluation was conducted with the aid of SHDB and the Social Hotspots Index (SHI; Benoît Norris et al., 2018), which calculates the social risks associated to the product and the supply chain according to Eq. (3), measured in medium risk hours equivalent (mrheq):

$$Social\ risks = Worker\ hours \cdot cost\ of\ the\ input \cdot indicator's\ risk\ level \tag{3}$$

Risk levels work as characterisation factors. These correspond to the risks of the country-sector in compliance with the variable measured in the indicator and the severity of a situation, the distribution of values across the population of countries and sectors and experts' judgement.

Table 4
Inputs for the S-LCA modelling (€) of the baseline and after-SSbD scenarios (BS: baseline scenario; S1: scenario 1; S2: scenario 2) for the annual production of doped ZnO (2.5 or 100 kg, depending on the scenario), using 1 kg of doped ZnO as the reference flow.

Industry	*BS*		*S1*[a]		*S2*	
	Austria	Germany	Austria	Germany	Austria	Germany
Chemicals	66.00	188.00	10.00	87.62	10.00	58.99
Labour	1440.00	–	1600.00	–	400.00	–
Electricity	4.00	–	3.84	–	2.88	–
Water	0.04	–	0.04	–	0.01	–
Bottles	–	200.00	–	100.00	–	10.00
Equipment	920.00	–	216.00	–	26.40	–
Transport	27.36	–	42.88	–	2.55	–
Corn	–	–	4.00	–	1.00	–

[a] In S1 some chemicals come from Brazil; such inputs amount to 23.78 €.

Table 5
Country-sector modelling and worker hours (wh) of the baseline and after-SSbD scenarios for the annual production of doped ZnO (2.5 or 100 kg, depending on the scenario), using 1 kg of doped ZnO as the reference flow.

Industry	Country-sector	wh (all scenarios)[a]
Chemicals	Chemical, rubber, plastic products (crp)/AUT U	1.09×10^{-5}
	Chemical, rubber, plastic products (crp)/DEU U	8.59×10^{-6}
	Chemical, rubber, plastic products (crp)/BRA U	–
Labour	Chemical, rubber, plastic products (crp)/AUT U	5.16×10^{-5}
	Phornano tailor-made worker hours (AUT)	1.39×10^{-7}
Electricity	Electricity (ely)/AUT U	4.08×10^{-6}
Water	Water (wtr)/AUT U	1.10×10^{-5}
Bottles	Manufactures nec (omf)/DEU U	5.27×10^{-5}
Equipment	Machinery and equipment nec (ome)/AUT U	2.58×10^{-5}
Transport	Transport nec (otp)/AUT U	2.81×10^{-5}
Corn	Cereal grains nec (gro)/AUT U	–

[a] All the shown data are common to BS, S1 and S2, with the exception of the chemicals coming from Brazil, which apply only to S1 (in this case, wh = 2.93×10^{-4}), and corn, applying only to S1 and S2 (in both cases, wh = 1.17×10^{-3}).

Then, these were aggregated for the different sub-categories and categories. Results were aggregated for each scenario (BS, S1 and S2) using the SHDB impact assessment method (SHI; Benoît Norris et al., 2018), which provides a single score in millipoints (mPt) based on the aggregation of the different sub-categories; this allows to compare the social performance of the product-system in the studied processes from a quantitative point of view. No weighting was applied to any indicator because of the uncertainties related to the innovative nature of the technology and its scale.

3.5.2. Approximations, assumptions and limitations

The background modelling for this case study was designed through an iterative process trying to understand which of the existing country-sector pair in the database would fit best the product-system; the chosen ones for each group are presented in Table 5. Regarding the country of origin of the machinery and equipment used, all the suppliers were assumed to be sited in Austria. Since there is no section accounting for labour impacts in the SHDB, a new one was included ('Phornano tailor-made worker hours').

The risks assessed in this case study come from the valuations included in the SHDB, which were adapted whenever possible to reflect Phornano's reality. Nevertheless, as the risk of a potentially occurring impact is measured according to macroeconomic measures, few risks were adapted; specifically, 'Unemployment level', as there were data not only for Austria altogether, but also for Korneuburg, the place in which the company is located.

3.6. Uncertainty analysis

Uncertainty analysis was performed with two purposes: (a) to evaluate the quality of data used in the foreground and background inventory, and price volatility. For LCA, MFCA and S-LCA, each scenario was evaluated considering the inputs variability. This has allowed to understand how input data uncertainties influence the final results, and thus support SSbD endeavours; (b) to use the calculated uncertainties to carry out a Multi-Criteria Decision Analysis (MCDA) (*Section 3.7*). For the environmental, economic and social assessments the SimaPro® 9.6 (2024) software was employed to conduct a Monte Carlo uncertainty analysis with 1000 runs. Two classes of uncertainties were considered: the basic uncertainty, which reflects the intrinsic variability, and the additional one, a consequence of the use of imperfect data (Santiago-Herrera et al., 2024). The basic uncertainty of input data was modelled through an *ad hoc* log-normal distribution representing the possible range of input values and the associated costs (*i.e.*, on raw materials, chemicals, energy, emissions of pollutants, equipment and labour) provided by Phornano. The additional uncertainty was determined through the Pedigree matrix. This matrix considers five quality indicators (reliability, completeness, temporal correlation, geographic correlation and further technological correlation) and, depending on the quality of the data sources, a score from 1 to 5 is assigned to each of them (Pizzol et al., 2024). An uncertainty factor was determined for each indicator and each score. All these values were added up, yielding SD_{g95}, according to Eq. (4) (Muller et al., 2016):

$$SD_{g95} \cong \sigma_g^2 = exp\sqrt{[ln(U_1)]^2 + [ln(U_2)]^2 + [ln(U_3)]^2 + [ln(U_4)]^2 + [ln(U_5)]^2 + [ln(U_b)]^2} \tag{4}$$

where U_1 = uncertainty factor of reliability, U_2 = uncertainty factor of completeness, U_3 = uncertainty factor of temporal correlation, U_4 = uncertainty factor of geographic correlation, U_5 = uncertainty factor of further technological correlation, and U_b = basic uncertainty factor.

For S-LCA, the Pedigree matrix was adapted to the particularities of this evaluation tool according to Mancini et al. (2018). The results of this matrix, translated into a single number employing Weidema et al.'s (2013) method in the absence of a specifically social translation model, built up the basic uncertainty of the social inventory, as it is inherited to the database functioning; the additional uncertainty for the social assessment was calculated based on the cost information inputted into the system.

3.7. Multi-Criteria Decision Analysis (MCDA)

In the literature, LCA, S-LCA and economic assessments are usually conducted separately for a given product, process, or service, and then the results for the different scenarios are compared. This works when the object of comparison is single indicators, but it is not trivial when multiple indicators are involved. In these cases, the user would need to compare each indicator of each domain for all the options considered which, besides being time-consuming, may introduce bias when interpreting the results and, therefore, in the selection of the most preferable alternative. To avoid this, performance of a Multi-Criteria Decision Analysis (MCDA) is advisable. According to Dean (2020), MCDA comprises various classes of methods, techniques and tools which explicitly consider multiple objectives and criteria in decision-making problems. Herein, a MCDA for the three Phornano scenarios was performed using the tool conceived by Prado and Heijungs (2018) and implemented by Tschulkow (2024). This is a straightforward tool that allows to easily access the results and includes Stochastic Multi-Attribute Analysis (SMAA), which ameliorates the balance between indicators.

For each of the three scenarios presented in this work, three indicators, *x*, *y* and *z*, representing the aggregated results of the environmental (LCA, *x*), economic (MFCA, *y*) and social (S-LCA, *z*) assessments, were considered. Briefly, the average value of each indicator, together with sigma, its standard deviation under 95 % interval confidence (SD_{g95}, or σ^2, which is defined in *Section 3.6*), obtained in the performed analyses (see *Section 4.4*), were entered in the Excel worksheet composed by Tschulkow (2024), which triggered a randomised 1000-iteration Monte Carlo simulation; this rendered the results, displayed as a 3-position ranking. Such results indicate how likely (%) is that each scenario is ranked first, second or third, 1 being the best-performing process from the sustainability point of view, 2 the second-best alternative and 3 the third-best option. Further analyses carried out between the two after-SSbD scenarios (S1 and S2) and between the most sustainable option and the baseline process follow the same pattern, but bearing in mind that in these cases the ranking consists of only two places. The Excel worksheet comprises nine tabs, which are described next. However, the development of this tool involves a deep mathematical reasoning, so the reader interested in it is referred to the mentioned work by Prado and Heijungs (2018). In addition, the authors recommend to check the MCDA worksheets included in SI ('MCDA_BS_S1_S2_comparison', 'MCDA_BS_S2_comparison' and 'MCDA_S1_S2_comparison') to follow the explanation:

- *Input parameters and results.* This step defines 3 alternatives (in this work, BS, S1 and S2) and 3 indicators by default (here, LCA, MFCA and S-LCA), although this can be modified *à la carte* (more or less alternatives, or more or less indicators) according to the analyses to be carried out. For instance, if two scenarios (*e.g.*, S1 and S2) are compared, the Excel worksheet needs to be adapted, removing data columns referred to the third process (BS), but keeping those involving the 3 indicators; the same applies if a 2-indicator analysis was to be conducted. Finally, the stochastic-based ranking results are provided.
- *Product indicator value (h).* In this step, the randomised values for each scenario and each indicator are generated based on the parameters (mean and standard deviation) defined in the 'Input parameters and results' tab. By default, 1000 Monte Carlo runs are performed.
- *Pairwise difference (d).* In this tab, the differences between pairs of the values generated in the previous step are calculated for a given indicator and each Monte Carlo iteration (*e.g.*, differences between BS and S1, BS and S2, and S1 and S2 for the LCA indicator).
- *Thresholds.* The preference (P_i) and indifference (Q_i) thresholds are calculated from the uncertainty values provided in the first tab, thus defining boundaries for the next step, the 'Outranking score'.
- *Outranking score (θ).* Here, pairs of alternatives (*e.g.*, BS *vs* S1, BS *vs* S2, or S1 *vs* S2) are compared to determine the preference or indifference of one with respect to the other, considering both pairwise differences and thresholds. If a given alternative (*e.g.*, S2) outperforms another (*e.g.*, S1), the preference is complete and such alternative (in this case, S2) gets an outranking score of 1. If the preference is weaker, it is called 'partial' and the outranking score for the reference alternative (in the example, S2) falls between 0 and 1. If the difference between alternatives is insignificant, then one alternative (S2) is indifferent with respect to the other (S1) and the score of the former is 0.
- *Net flows (π).* The values of the outranking scores obtained in the previous step for each Monte Carlo run are compared from the inverse angle. Following with the example, is S2 completely preferable, partially preferable or indifferent regarding S1, and is S1 completely preferable, partially preferable or indifferent with respect to S2? Positive values show how much the reference alternative (S2) outranks the other (S1), whereas negative ones indicate how much the former (S2) is outranked by the latter (S1).
- *Weights (w).* This weighs the relevance of each indicator. However, assigning a weight requires preference information that is often unavailable. In these cases, it is advisable to use stochastic weights to reflect the lack of knowledge about those weights, specially when analysing a low-TRL technology. Thus, weight factors ranging between 0 and 100 and amounting to 100 are randomly calculated for each Monte Carlo iteration.
- *Overall score (z).* In this tab, the overall ranking for each Monte Carlo run is calculated through a weighted sum of the net flows and the weight factors. Then, alternatives (BS, S1 and S2) are ranked according to their overall score.
- *Rank (r).* A counting per Monte Carlo iteration of the rank of each alternative is done based on the results of the previous step. This generates a probabilistic rank that allows to establish the likelihood of BS, S1 and S2 to occupy the first, second or third position of the ranking, and therefore compare their performances.

Beyond determining the likelihood of a certain scenario to be placed in one or another position of the ranking, the performance of the studied processes in a particular indicator (in this work, LCA, MFCA or S-LCA) was assessed. Once the 1000-iteration Monte Carlo simulation was run, a stochastic outcome of the three processes based on the three indicators was generated (this corresponds to the 'Product indicator value (h)' step previously defined); the lower the average value of the indicator, the more preferable the process is, as it would be less impactful. Given the early stage of this technology, no weighting was applied to any indicator.

Despite this, a sensitivity analysis was conducted to understand the impact of using randomly generated weights or manually fixed ones in the final result. The former were obtained through a 1000-iteration Monte Carlo simulation, whereas pre-defined weights were introduced in the 'Weights (w)' tab of the Excel worksheet, in such a way that the three indicators had either the same relevance in the analysis (33.33 % each), or one of them was given preference over the other two, with the latter displaying identical values. For instance, a 40 % weight was assigned to the environmental indicator, and a 30 % weight was attributed to each of the remaining ones (economic and social), the sum of all the items being 100 %. This procedure was repeated, but prioritising either the economic or the social indicator (40 % weight), with the other two having lower but similar values (30 % each). This analysis was performed again, but increasing the weight of the prioritised indicator (60 %, 80 % and 90 %) and, consequently, decreasing the weight of the other two (20 % each, 10 % each and 5 % each, respectively).

4. Results and discussion

4.1. LCA results and interpretation

The results for the Environmental Footprint indicators outlined in *Section 3.3.3* corresponding to the three scenarios reported in this study are presented in Tables 6 and S1–S3, and Figs. 5 and S1–S3; for a deeper information, please refer to the 'LCA_Results' worksheet of the SI. As shown in Table 6, the redesigned production of 2.5 kg of doped ZnO (S1) outperforms the initial design (BS) for eight environmental indicators and, looking at the single score, it allows a reduction of the overall impact of more than 50 % (6.6 mPt instead of 13.7). Regarding S2, it outperforms even better the baseline scenario for ten environmental indicators (including, *e.g.*, climate change, ozone depletion, particulate matter, acidification, and ecotoxicity, freshwater). Looking at the single score, it offers a reduction of the total aggregated impact by 67 % (4.4 mPt instead of 13.7 initially). The improvement of the environmental

Table 6

LCA results for each scenario (BS: baseline scenario; S1: scenario 1; S2: scenario 2). The red-yellow-green pattern, in this order, indicates a progressive reduction of the environmental impacts.

Damage category (EF 3.1)	Unit	*BS*	*S1*	*S2*
Climate change	kg CO_2 eq	7.99	9.92	6.90
Ozone depletion	kg CFC11 eq	6.00×10^{-7}	2.17×10^{-7}	1.57×10^{-7}
Ionising radiation	kBq U-235 eq	2.72×10^{-1}	9.36×10^{-1}	6.64×10^{-1}
Photochemical ozone formation	kg NMVOC eq	1.14	5.78×10^{-1}	3.87×10^{-1}
Particulate matter	disease inc.	2.10×10^{-6}	1.29×10^{-6}	8.60×10^{-7}
Human toxicity, non-cancer	CTUh	7.24×10^{-8}	1.56×10^{-7}	1.08×10^{-7}
Human toxicity, cancer	CTUh	1.49×10^{-9}	4.40×10^{-9}	2.96×10^{-9}
Acidification	mol H^+ eq	8.80×10^{-1}	4.72×10^{-1}	3.16×10^{-1}
Eutrophication, freshwater	kg P eq	6.04×10^{-4}	4.49×10^{-3}	3.10×10^{-3}
Eutrophication, marine	kg N eq	4.49×10^{-1}	2.26×10^{-1}	1.50×10^{-1}
Eutrophication, terrestrial	mol N eq	4.96	2.57	1.72
Ecotoxicity, freshwater	CTUe	5.11×10^{3}	6.49×10^{1}	3.13×10^{1}
Land use	Pt	9.24×10^{2}	5.32×10^{1}	2.95×10^{1}
Water use	m^3 depriv.	3.62	5.84	2.98
Resource use, fossils	MJ	8.96×10^{1}	1.26×10^{2}	8.99×10^{1}
Resource use, minerals and metals	kg Sb eq	2.78×10^{-6}	1.12×10^{-4}	7.89×10^{-5}
Single score	**mPt**	**13.7**	**6.6**	**4.4**

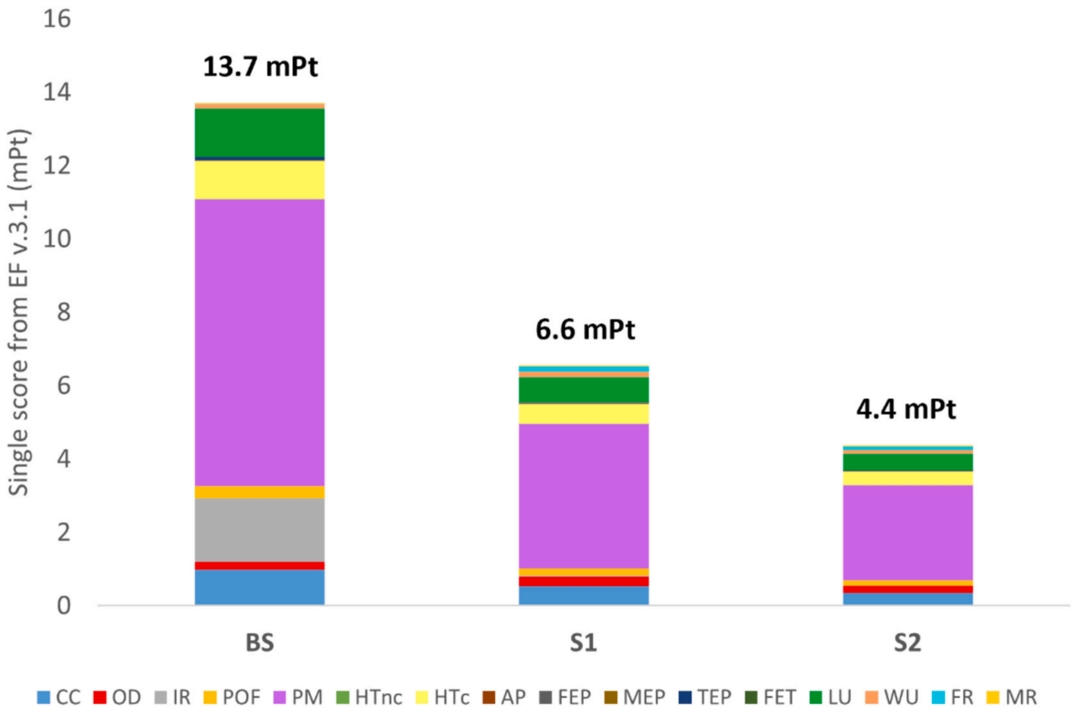

Fig. 5. Comparison of the overall ecological footprint of the three scenarios (BS, S1 and S2) considering the 16 analysed environmental indicators (CC = climate change; OD = ozone depletion; IR = ionising radiation; POF = photochemical ozone formation; PM = particulate matter; HTnc = human toxicity, non-cancer; HTc = human toxicity, cancer; AP = acidification; FEP = eutrophication, freshwater; MEP = eutrophication, marine; TEP = eutrophication, terrestrial; FET = ecotoxicity, freshwater; LU = land use; WU = water use; FR = resource use, fossils; MR = resource use, minerals and metals). The single score obtained for each scenario is indicated above each bar.

results, both in terms of single score and of the above-mentioned indicators, in the redesigned scenarios is also observed in Fig. 5.

To better understand the source of impacts, the relative contributions of production flows for both redesigned scenarios are displayed in Figs. S2 and S3. The direct emissions from the production process have significant impacts on several indicators. Indeed, the release of NO_2 contributes to the impacts on photochemical ozone formation, particulate matter, acidification, as well as marine and terrestrial eutrophication. The various impacts of this substance highlight the benefits of converting it to HNO_3 after the application of the indicated SSbD strategies (*Section 3.1*). Indeed, as quantified and elaborated through the aforementioned LCA results, reducing the quantity of NO_2 released to the air in S1 and S2 allowed to significantly mitigate the environmental impact in the five environmental impact categories.

Regarding the other impact categories for the two redesigned scenarios, there are three main drivers: the production of HNO_3 (main mass flow input), of $Zn(NO_3)_2{\cdot}6H_2O$ (under S1) or zinc powder (under S2), and of electricity.

The supply chain of HNO_3 significantly affects (more than 25 % of total impacts) climate change, ozone depletion, carcinogenic human toxicity, water use and resource use (fossils, minerals and metals). Concerning $Zn(NO_3)_2{\cdot}6H_2O$, its synthesis generates impacts mainly on non-carcinogenic human toxicity, ozone depletion, fossil resources depletion, climate change and water use. These impacts come both from the production of ZnO and HNO_3, in particular the use of energy to produce these precursors as well as water losses (for water resources depletion impact). It must be noted that the quantity of $Zn(NO_3)_2{\cdot}6H_2O$ employed in the redesigned scenarios was significantly diminished and mostly substituted by zinc powder and HNO_3. Regarding electricity, the main contributions were identified on freshwater eutrophication, ionising radiation, fossil resources depletion, climate change, ozone depletion and resource use, due to the shares of electricity from coal/lignite (about 16 % of the Austrian mix), nuclear (about 7 %) and natural gas (about 11 %). The consumption and disposal of water has quite low impacts, the main ones being on freshwater ecotoxicity due to metals release to water or soil (from sludge disposal), whereas the transport of materials does not generate significant impacts.

The work reported in this section is a clear display of the usefulness of ex-ante LCA to identify and address the environmental challenges associated with a given manufacturing process, in this case the original production scenario (BS) of ZnO NPs. The assessment provided critical insights into areas that required improvement, revealing key environmental shortcomings of BS, such as significant emissions of SO_x and NO_x and the lack of circularity in material flows. As explained above, the development of S1 and S2 showed substantial advancements from the environmental viewpoint, and, as it will be shown next, they are crucial for the sustainability of the synthetic process. By prioritising the reduction of harmful emissions and promoting material reuse, the redesigned scenarios demonstrate the strategic value of ex-ante LCA in fostering sustainable innovations that meet both market and policy demands (*Section 4.6*). However, as for other ex-ante LCA studies (Tan et al., 2018; Pallas et al., 2020; Nizam et al., 2021; Müller-Carneiro et al., 2023), the accuracy of the assessment heavily relies on assumptions about future scenarios and the availability of reliable data. Besides, unknown final function, complexity of the scale-up procedure, and uncertainty are identified as the main challenges for ex-ante LCA (Röder et al., 2022), and in this case in particular the actual/real use/release of NMs in the environment still need to be observed/monitored in real-life application, which only have been modelled in the ex-ante LCA here. To address these limitations, further studies are required to validate the predictions through post-implementation evaluations.

4.2. MFCA assessment results and interpretation

Tables 7 and S4–S6, and Figs. S4–S6, display the detailed results of the MFCA analyses carried out for the three scenarios (BS, S1 and S2), reporting both the annual cost of each cost driver and the costs per kg of doped ZnO nanopowder (this can also be found in the 'MFCA_Results' worksheet of the SI). The input expenses were converted into two distinct output cost categories, profitable and waste cost. The former is associated with the output flows that represent a possible profit for the company by leading to a saleable final product, whereas the latter, as the name suggests, are the expenses due to discarded flows along the production line.

A comparative graphical depiction of the overall costs of producing the doped ZnO nanopowder according to BS, S1 and S2 is displayed in Fig. 6. A breakdown of the cost inputs is given, as well as their outcome as either a profitable cost or waste cost of production.

Compared to BS, in S1 there is an overall reduction of 5 % in production cost, or 117 €/kg of ZnO. Similarly to the original process, the main cost driver and hotspot in the first redesigned scenario is the labour input. In fact, labour expenses have increased from representing 65 % of the total production cost to 77 %, which is mainly due to an increase in the hourly labour rate reported by the firm. Elsewhere, changes in the packaging have reduced expenses with the bottles, decreasing from 200 €/kg of ZnO (9 % of total cost) to just 100 €/kg of ZnO (5 %). Equipment calibration costs, unchanged from BS, are the second most important cost driver (8 %) in S1. In terms of raw materials, the changes in the production process (*Section 3.1*) have led to a reduction in the amount of employed $Zn(NO_3)_2{\cdot}6H_2O$, the elimination of whey and the introduction of non-aminated starch, zinc powder and HNO_3. These show promising results in terms of production cost, with a reduction from 254 € of raw materials/kg of ZnO to just 125 €. Raw material inputs now account for just 6 % of the total cost. Since the non-aminated starch presents a very small contribution to the overall production costs, too small to be observed in the bar chart, it was grouped in the 'Others' category for S1 and S2 in Fig. 6. This was also done for other inputs, namely the deionised water (in BS and S1), the tap water (all scenarios) and the electricity input (all scenarios).

Regarding waste costs, the reduction of the nanoparticle amount that is lost *via* wastewater due to the cleaning procedures and packaging steps also leads to considerable cost savings, from 231 €/kg of ZnO in BS down to 52 € in S1, just 2.5 % of the total.

Advancing to the upscaled process (S2), the large decrease in production costs/kg of ZnO is clear, both when compared to S1 and BS (reduction of 75 and 77 % in final cost, respectively, down to 512 €/kg of ZnO). Notwithstanding the process modifications, the cost distribution *via* the different cost drivers assumes a similar profile to that of S1. Labour costs are still by far the most prominent expense, accounting for 78 % of the total (400 €/kg of ZnO). Other than HNO_3 (the second highest cost driver at 8 % of the total), the remaining costs are evenly spread between the other raw material inputs like $Mn(NO_3)_2{\cdot}4H_2O$, reactor equipment costs, the bottles for packaging, process water and the zinc powder. The breakdown between profitable and waste cost also shares similar values to S1, with waste costs representing 2.5 % of the total. Overall, as for LCA, these results confirm the success of the applied SSbD measures. Comparisons of these findings with published literature are difficult, since existing publications analysing the economic viability of ZnO NPs production refer to different temporal boundaries, geographical regions and production processes (Nurahmawati and Nandiyanto, 2015; Zahra et al., 2020). Issues like these, which prevent comparative analyses, add to the lack of a common methodological framework and the inherent complexity of economic assessments, which, in this case study, mainly lies in the lack of data/analysis of the use and end-of-life phases, and in the temporal boundaries, as only the present costs (2022–2024) were considered, with no projections for future market developments or technological maturity. But, despite these limitations, MFCA is a valuable standardised tool to perform the economic analysis

Table 7
MFCA results (€) for each scenario (BS: baseline scenario; S1: scenario 1; S2: scenario 2).

Scenario	Annual profitable cost	Profitable cost/kg of ZnO nanopowder	Annual wasted cost	Wasted cost/kg of ZnO nanopowder	Annual total cost	Total cost/kg of ZnO nanopowder
BS	4937	1975	576	231	5514	2206
S1	5090.87	2036.35	129.51	51.80	5220.38	2088.15
S2	49,875	498.75	1308	13.08	51,183	511.83

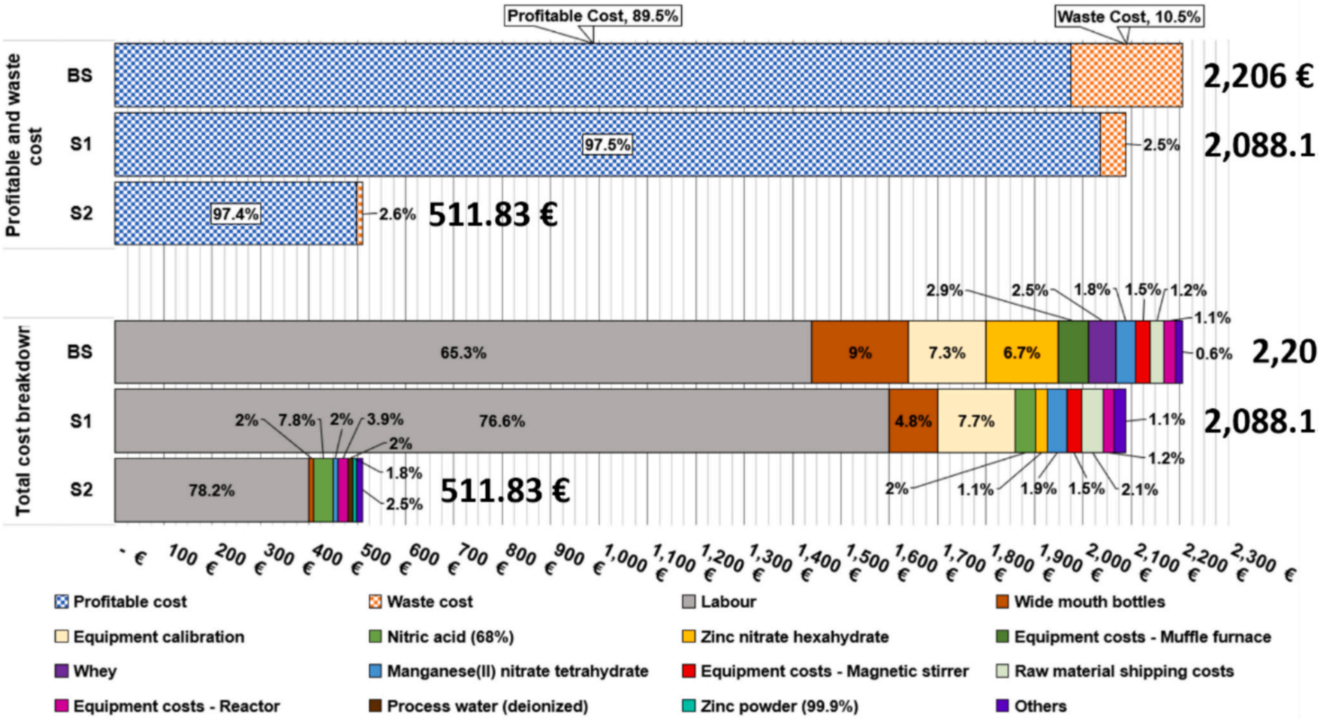

Fig. 6. Comparison of the overall costs of manufacturing doped ZnO nanopowders through the three scenarios (BS, S1 and S2), in terms of profitable and waste cost (top) and total cost breakdown (bottom). The total production cost for each scenario is indicated above each bar.

Table 8
S-LCA results (mPt) for each scenario (BS: baseline scenario; S1: scenario 1; S2: scenario 2) and reduction (%) of the most impactful subcategories.

	BS	*S1*	*S2*
Total score (mPt)	158.9	82.0	20.9
Most impactful subcategories (%)			
Injuries and fatalities	100	47	88
Democracy and freedom of speech	100	48	88
Wage assessment	100	48	88
Forced labour	100	49	87
Discrimination	100	50	87
Occupational toxics and hazards	100	51	87
Excessive working time	100	50	88

of a given process, since it allows identifying inefficiencies and quantifying material and energy losses, facilitating decision-making towards resource optimisation and costs savings. Most importantly, MFCA is aligned with the SSbD methodology, as it permits to evaluate the economic impact of various alternatives, such as those described in this work, promoting improvements in resource efficiency and reduction of environmental footprint.

4.3. S-LCA results and interpretation

The presented results (Tables 8 and S7–S15, and Fig. 7; for a more detailed information, the reader is referred to the 'S-LCA_Results' worksheet of the SI) show that the application of SSbD strategies to the original synthetic process led to a remarkable reduction of the social footprint of the complete product-system: around 48 % from BS to S1 scenario, and about 87 % from BS to S2. As observed for BS, in the after-SSbD scenarios the most impactful category remains 'Labour rights'. However, if subcategories are considered, it is 'Injuries and fatalities', within the category 'Health and safety', the most impactful one, followed by 'Democracy and freedom of speech', within the category 'Governance'. These results show that even in a product-system set in a country (Austria) that scores 0.91 out of 1 in freedom of speech (V-Dem Institute, 2024) and 0.89 out of 1 in democracy, according to the Democracy Matrix Index (Democracy Matrix, 2024), these are still hotspots across the product-system value chain. Therefore, an eye should be kept on the suppliers and their power dynamics in third-party countries.

As for 'Injuries and fatalities', Austria ranks 18/78 in the ILO statistics for number of occupational injuries per 100,000 employees, and 34/78 in fatalities per 100,000 workers, being the third European country with a higher number of fatalities, only behind Latvia and Malta (ILOSTAT, 2024). The qualitative questionnaire (see the 'S-LCA_Results' worksheet of the SI) answered by Phornano aiming at identifying hotspots related with the health and safety of the employees confirmed that there are no signs of potentially harmful or problematic behaviour within the company. Nevertheless, there is a risk upstream the value chain and, consequently, tighter control of their suppliers' compliance with employment regulation and safety legislation would be beneficial.

For the most impactful subcategories (Table 8), S1 allows a reduction of almost 50 % of the risk, while scaling up the production would lead to a dramatic drop of the risk (almost 88 % for those subcategories). Nevertheless, it must be noted that this methodology does not consider the consequences that the production of Mn-doped ZnO NPs in a commercial level would entail for macroeconomic scope. Handy and Shaw (2007) analysed the social impacts of NMs, concluding that hotspots are specific to a certain end use and specific components within the material, which limits comparability of S-LCA results and justifies the sparsity of literature on the topic, particularly for low-TRL applications. Nevertheless, the existence of hotspots related to workers' health and safety is predominant in literature on social implications of NMs (Megahed, 2014; Vavra et al., 2014), confirming the results obtained in the ZnO NPs case study.

Considering the contribution of the different inputs to the global social impact, the original design's footprint was driven by the huge contribution of social risks associated with equipment, which accounted for over 58 % of the total. Improvement of the production process *via* the above-mentioned measures (*Section 3.1*) led to a noteworthy decrease of such contribution, turning out to be *ca.* 36 and 17 % for S1 and S2, respectively. Again, this confirms the suitability of the applied SSbD

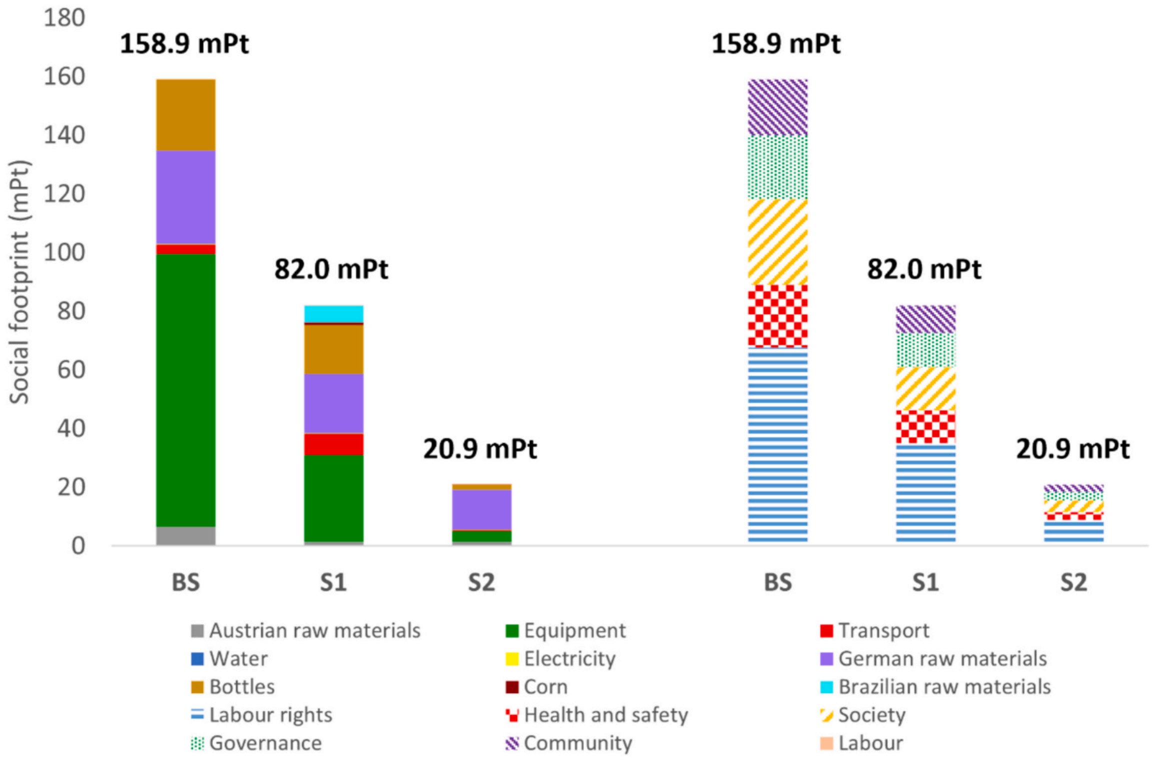

Fig. 7. Comparison of the social footprint of the three scenarios (BS, S1 and S2) per input (left) and impact category (right) (in mPt). The single score obtained for each scenario is indicated above each bar.

strategies. However, the share of risks associated with bottles and raw materials coming from Germany increases in S1 and S2. Nevertheless, in absolute terms, the social performance of these inputs has also improved in S1 and S2. This difference is due to the intrinsic nature of performing database-assisted S-LCA analyses, which rely on commodities' markets dynamics (Alsamawi et al., 2017). These multi-regional input-output models and their outcomes are not tailor-made for pilot scale, highly specialised intermediate products, and their specificities. To exemplify this, the contribution of equipment manufacturing to the total social footprint decreases around 70 % in S2 with respect to BS. The sourcing of German raw materials (contributing to 20 % of the impact in BS) becomes the main driver of the total footprint in S2 (contributing to around 65 % of the social footprint) just because it has not remained almost the same while the impacts from the rest of the product-system have decreased. Overall, as in LCA and MFCA, these results confirm the success of the proposed redesign strategies.

Application of a database-assisted S-LCA in low TRLs can help to operationalise and advance the socio-economic impact measurement methods within the SSbD framework, an area that this approach has left open to different interpretations. Nevertheless, application of S-LCA in low-TRL cases has some limitations. For instance, this methodology is hindered by a critical shortage of reliable, context-specific social data that forces reliance on generalised proxy indicators (Siebert et al., 2018). Other challenges arise from misapplication of traditional functional units (Macombe et al., 2018) and linear scaling assumptions that fail to reflect dynamic social realities (Reinales et al., 2020), as well as from inherent epistemological uncertainties and ethical dilemmas, which undermine the objectivity and reproducibility of assessments (Sakellariou, 2018; Tragnone et al., 2022), collectively limiting the robustness and practical applicability of S-LCA for early-stage technological innovations (Macombe et al., 2018). Acknowledgement of these limitations allows a critical use of the insights generated through the evaluations, which can benefit an informed decision-making. Specifically, for SSbD, using a database-assisted S-LCA method as a screening tool (Pizzol et al., 2023) helps to get a general outlook of what materials are better to avoid from the social perspective, and which suppliers are better to audit closely, providing a relevant decision tool when selecting different design alternatives and when dealing with supply-chain management.

4.4. Uncertainty analysis results

SD_{g95} values were calculated according to the procedure described in *Section 3.6*; the results for each assessment (environmental, economic and social) and each scenario are displayed in Table 9. For LCA, Nizam et al. (2021) report that 92 % of NMs LCA studies published between 2001 and 2020 neglected any uncertainty analysis. This reflects the necessity of performing these analyses to complete environmental assessments, but at the same time shows the difficulty of obtaining robust uncertainty values. For the LCA presented here, both the uncertainty and

Table 9
Aggregated results and their global uncertainties (SD_{g95}) resulting from the environmental (Pt), economic (€) and social (Pt) stochastic processes carried out for each scenario (BS: baseline scenario; S1: scenario 1; S2: scenario 2).

Indicator	*BS*		*S1*		*S2*	
	Mean	SD_{g95}	Mean	SD_{g95}	Mean	SD_{g95}
Environmental	0.0156	0.0049	0.0107	0.0037	0.0072	0.0010
Economic	2205	18	2088	11	512	3
Social	0.1585	0.0164	0.0823	0.0062	0.0209	0.0023

sensitivity analyses conducted, even on the most sensitive parameters, do not impact the interpretation of the outcome of the evaluation, with S2 being an environmentally friendlier scenario than S1 and BS (see *Section 4.5*), but SD_{g95} values are high (between 14 and 35 % of the mean values). However, it should be noted that performing a 'cradle-to-gate' LCA involves the compilation of data from external sources, including databases, and relies on assumptions and approximations, which, taken together, increase the complexity of the analysis and its uncertainty. The same applies to the social assessment, although in this case the calculated SD_{g95} values are lower (about 10 % of the mean values); when interpreting these results, it should also be noted that Type I S-LCA, the one performed in this work, can only provide risks of impacts happening and not actual impacts. Comparatively, MFCA uncertainties are quite low (less than 1 % with respect to the average cost values for each scenario), which is understandable: the information used to conduct this assessment is more accessible, because it relies on internal data which depend to a lesser extent on estimates or external sources, such as databases, thus increasing the precision of the analysis. Anyway, as pointed out for LCA, the uncertainty studies performed for the socio-economic assessment do not alter the global result of the work.

Altogether, showcasing the hotspots of the technology allows addressing potential issues of uncertainty when scaling up such technology, thus easing decision-making and contributing to issues related to the application of SSbD (Abbate et al., 2025).

4.5. Integration of the aggregated results: Multi-Criteria Decision Analysis (MCDA)

The LCA, MFCA and S-LCA results for the investigated Phornano alternatives (BS, S1 and S2) were integrated into a Multi-Criteria Decision Analysis (MCDA) to conclude which of the three options was the most preferable from the sustainability point of view. The values obtained for each indicator (environmental, x; economic, y; social, z) for each alternative, and their uncertainties, calculated as explained in *Section 3.6* (Table 9), were introduced in the selected tool (*Section 3.7*). After performing a 1000-iteration Monte Carlo analysis, a 3-position ranking was obtained (Fig. 8a). It is clear that the best-performing option from the sustainability viewpoint is S2, with almost 100 % likelihood. The most likely alternative to be ranked second is S1 (around 96 % probability) and BS would be the third-best option (about 97 % likelihood). This confirms the advantage of the redesigned scenarios, in particular of S2, against the baseline option. The results displayed in this section are presented in detail in the MCDA worksheets of SI ('MCDA_BS_S1_S2_comparison', 'MCDA_BS_S2_comparison' and 'MCDA_S1_S2_comparison').

The performance of the three scenarios, BS, S1 and S2, in each indicator (environmental, x; economic, y; social, z) was also explored. It should be noted that, given the lack of the required information to attribute weights to those indicators (a consequence of the low TRL of this technology), the generation of randomised stochastic values was regarded as the most suitable option for this study. Introduction of the values of the aforementioned indicators (x, y and z) and their

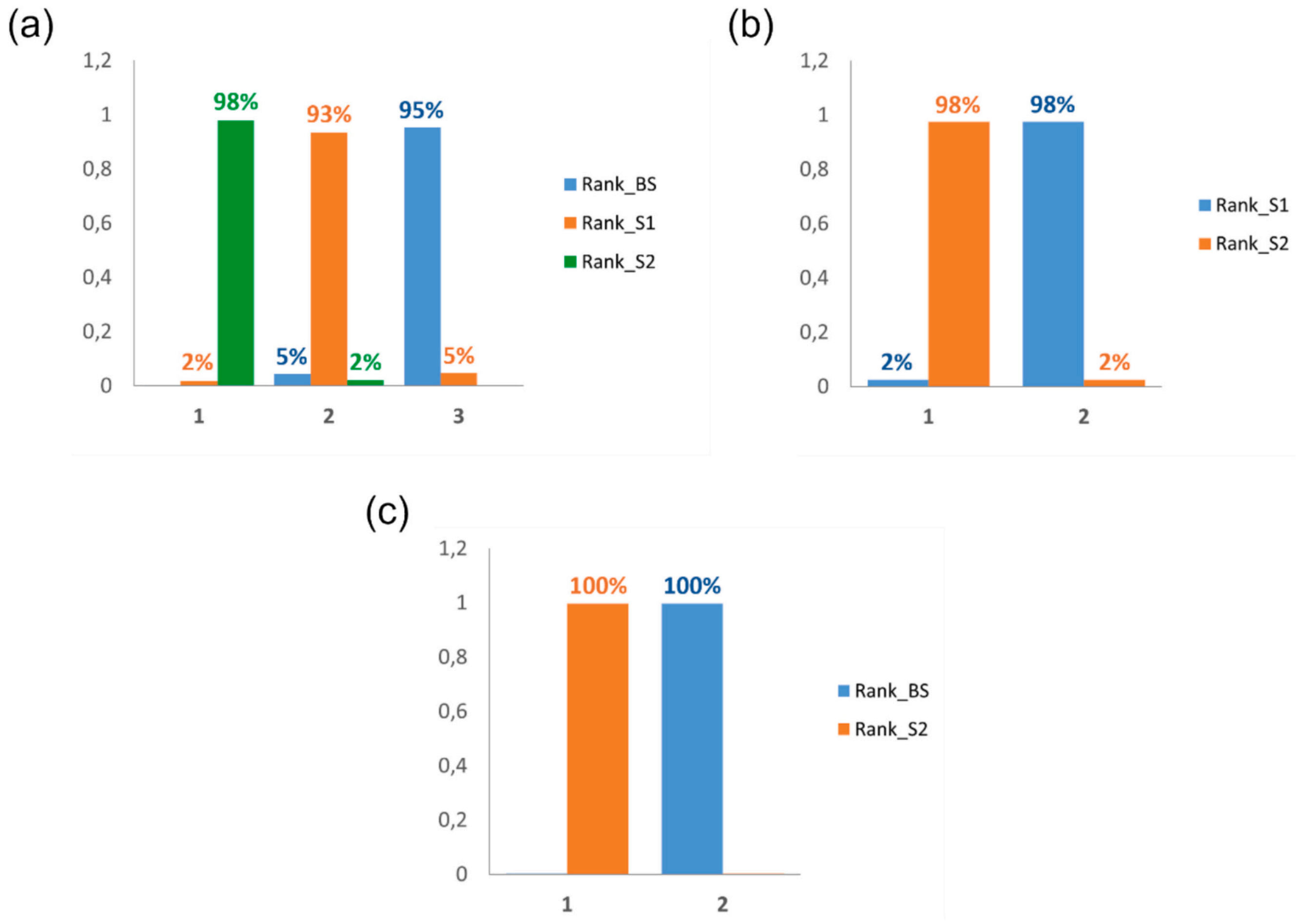

Fig. 8. Ranking obtained after conducting the MCDA for: (a) the three-option (BS, S1 and S2) Phornano case study; (b) a two-option (S1 and S2) Phornano case study; (c) a two-option (BS and S2) Phornano case study. The Y axis represents the probability and the X axis the ranking position. The probability of each scenario to occupy the first, second or third position of the ranking is indicated, as a percentage, above each bar.

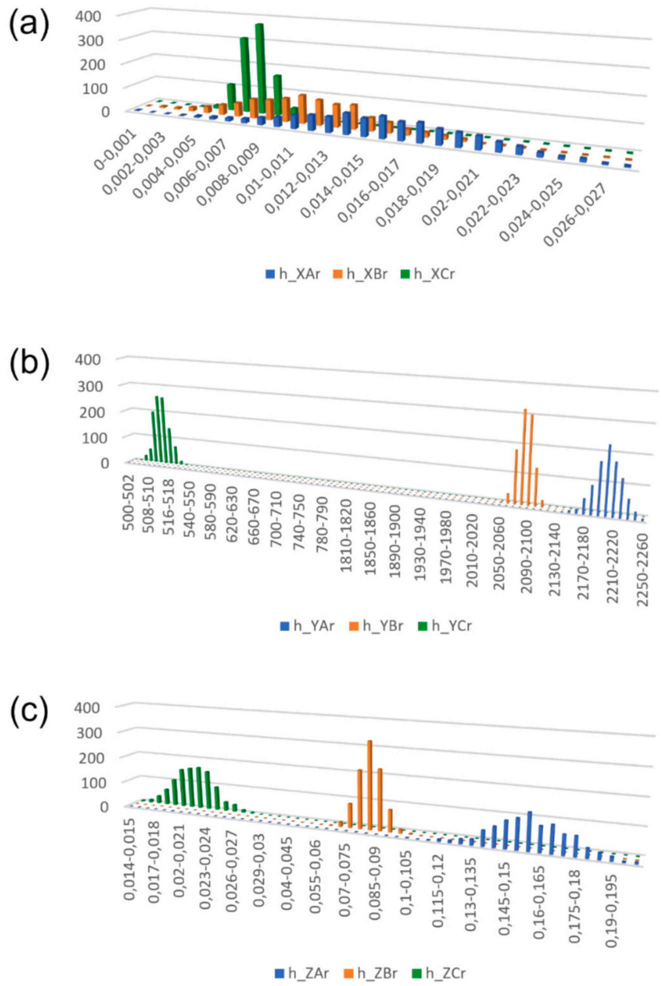

Fig. 9. Analysis of the performance of options A (baseline scenario, BS), B (2.5-kg redesign, S1) and C (100-kg scaled-up process, S2) in each indicator: (a) environmental, *x*, (b) economic, *y* and (c) social, *z*, for the Phornano case study. The Y axis represents the frequency of the corresponding range (X axis) resulting from the Monte Carlo analysis, and the X axis the Pt (environmental and social indicators) or € (economic indicator) of the analysed scenarios.

uncertainties (Table 9) in the Excel worksheet triggered a 1000-iteration Monte-Carlo simulation. This means that, for each scenario and each indicator, 1000 values are randomly generated, and their average and standard deviation calculated. These numbers can be grouped by ranges; if the frequency of appearance of those ranges in the stochastic analysis is plotted against such ranges, Gaussian-like distributions are obtained, with their profile (shape or broad) depending on the uncertainty of the initial values. Hence, the distributions obtained for the three scenarios for a given indicator can be represented in the same graph, to compare the performance of the studied processes from the environmental, economic and social viewpoints. The results of this analysis for the three scenarios and the three reported indicators are shown in Fig. 9. Environmentally, S2 is the scenario with the lowest score (roughly 0.007 Pt), followed by S1 (around 0.011 Pt) and, finally, BS, with approximately 0.016 Pt (the average values resulting from the stochastic processes were considered; see Table 9). This means that the impacts generated when producing 1 kg of doped ZnO through S2 are less than half of those originated *via* BS, and 1.5 times lower than those generated by S1. Concerning the costs of such manufacturing, S2 is, by far, the most affordable option. Although S1 is less expensive than BS (2088 € *vs* 2205 € on average), S2 (512 €) is roughly four times cheaper than the other two. Finally, S2 is also the least impactful process from the social point of view (0.021 Pt *vs* 0.082 Pt –S1– and 0.158 Pt –BS–). The results for the three indicators considered individually are in agreement with the main outcome of the MCDA: the 100-kg scaled-up scenario, S2, is the most sustainable of the three proposed options. In addition, S1 performs better than BS in the three indicators, which makes it the second most sustainable process of the study.

After conducting this research, two additional MCDAs were proposed, each of them consisting of two scenarios, to confirm the above-presented results: on the one hand, a study between S1 and S2 and, on the other, between the best-performing redesign resulting from this analysis and BS.

The ranking obtained from the first of the two proposed MCDAs is shown in Fig. 8b. S2 is the most sustainable process. Indeed, this is the alternative that is more likely to occupy the first position (around 98 % likelihood), the chances of S1 to be ranked first being negligible. Therefore, the latter would be ranked second. This outcome is in line with that obtained from the former MCDA. In a similar fashion, the behaviour of S1 and S2 in the environmental (*x*), economic (*y*) and social (*z*) indicators was explored (Fig. S7). With respect to the former, S2 is 1.5 times less impactful than S1, whereas the cost of S2 is remarkably lower than that of S1 (around 512 € *vs* 2088 €). Finally, the social impacts derived from the production of 1 kg of doped ZnO NPs through S2 are *ca.* 4 times lower than those generated by S1. Altogether, these results match those of the current MCDA and of that considering the three scenarios, where S2 was preferred over S1.

Given this result, the next MCDA that was performed is that between BS and S2. Introduction of the values obtained for each indicator for both alternatives throwed the results presented in Figs. 8c and S8. Again, S2 is the best-performing process from the sustainability point of view (nearly 100 % likelihood), so the original design, BS, would be the least advisable process to produce 1 kg of doped ZnO NPs. This is also reflected in the indicators. Indeed, when studying the environmental impacts, S2 is roughly twice less impactful than BS, whereas in terms of social impacts the ratio is around 8:1 (BS:S2). Economically, S2 is also preferable, given that the cost of manufacturing 1 kg of doped ZnO NPs is 512 € in the case of S2 and 2205 € in the case of BS, on average. All of this makes S2 a superior option, in agreement with the current and former MCDAs. Thus, the 100-kg scaled-up scenario, in which circular economy principles were followed to reduce some raw materials inputs, is the most sustainable one of the three that have been studied in this work.

Although at this stage of the research it was not possible to assign weights to the environmental, economic and social indicators, a sensitivity analysis was carried out to understand the impact of fixing weights in the analysis, instead of using randomly generated ones, considering either that the three indicators are equally relevant (33.33 % weight assigned to each one), or giving preference to one of them over the others, according to the procedure described in *Section 3.7*. The results, shown in SI (Fig. S9), allow to conclude that the global outcome depends neither on the nature of the weights, nor on the priority of one of them over the other two, as in all cases the trend is similar to that shown in Fig. 8, with S2 being the most likely process to be ranked first from the sustainability viewpoint, followed by S1.

As indicated in *Section 2*, the literature about application of MCDA tools to analyse the holistic sustainability of NMs production processes is scarce, and no works focused on ZnO NPs have been found. Anyway, potential comparisons are difficult due to the different nature of collected data (qualitative or quantitative) and settings/tools (Hansen, 2010). It should be noted that, while MCDA proves to be a highly effective tool to visualise results and support decision-making in a process evaluation, as shown in this work, it is crucial to keep the interpretation of results separately for the three sustainability pillars. This ensures that potential trade-offs among these dimensions are explicitly recognised and mitigated, avoiding unintended compensations that could compromise truly sustainable outcomes. That said, the SSbD framework recommends the use of MCDA to evaluate and compare several alternatives, considering safety and sustainability factors

(Abbate et al., 2025). Particularly, MCDA allows for balancing complex trade-offs among environmental, social and economic criteria. This integration is in line with SSbD principles, as this methodology provides a solid foundation for decision-making from the earliest stages of development.

4.6. *ZnO NPs: policy implications and commercial prospects*

As this work is the result of a EU-funded research project, European policies concerning NMs have been considered to carry out this investigation. In this context, the EU's environmental regulations (*e.g.*, REACH; European Commission, 2006) require NMs producers to evaluate and limit the impacts derived from the manufacture of these materials. As explained in *Section 2*, emissions of NPs during the production of these goods is a topic of special concern, so efforts to study the mechanisms accounting for their release and to determine their characterisation factors are being prioritised. By the same token, the EU is pushing for the adoption of cleaner, safer and more efficient methods to synthesise NPs. The SSbD framework (European Commission, 2022) is a voluntary approach to guide the innovation process for chemicals and materials. This work is a case study that explores the applicability of this framework and provides insights for further definition, with a particular focus on NMs, given their singular characteristics.

As a result of this approach, significant conclusions to improve the production process of ZnO NPs have been ideated. The so-called 'French process', consisting in the vaporisation of metallic Zn followed by its oxidation with air at high temperatures and rapid cooling of the formed ZnO particles, is a typical way to obtain this product (Charnhattakorn et al., 2011). However, it is an energy-intensive method, and getting particles of uniform size is not trivial. In contrast, the processes presented in this work are environmentally friendly, in line with the EU's Green Deal (European Commission, 2019), and controlling particles size is easier. Monitoring of the exposure of workers to NMs is also critical, as it may pose health risks, such as respiratory problems; thus, compliance of the manufacturing processes with the EU's legislation on this subject (European Commission, 2006) and the European Chemicals Agency (ECHA) is mandatory.

From the commercial perspective, the market for ZnO NPs is expected to grow significantly in the near future, from USD 254.4 million in 2020 to USD 425.2 million in 2027, representing a Compound Annual Growth Rate (CAGR) of 7.6 % (Chandrasekaran et al., 2024). ZnO NPs are currently used in several industries and products. Besides personal care goods, particularly sunscreens, wastewater treatment and biomedical devices are common applications of this material. Nonetheless, further research is necessary to improve its production and enhance its commercial viability and thus explore new opportunities to access untapped markets (Goswami et al., 2024). The scenarios studied in this *paper* allow to synthesise ZnO particles of nanometric size, which, in relation to the mentioned sunscreens, are more efficient in blocking UV light than microparticles (Kumari et al., 2010), that can result from the 'French process': if both sizes are compared, less NPs are needed to achieve a similar effect, which presents a clear commercial interest. Altogether, collaboration between academia, industry and regulatory bodies is key to boost commercialisation and technological innovations of ZnO NPs (Xie and Wang, 2021).

5. Conclusions

In this work the Environmental, Economic and Social Life Cycle Assessments (LCA, MFCA and S-LCA, respectively) of three processes aimed at the production of Mn-doped ZnO NPs, complemented with a Multi-Criteria Decision Analysis (MCDA) to objectively decide which of them was the most sustainable one, were presented. According to the thorough literature review that was carried out, this is the most complete work in this field to date.

The original production scenario conceived by Phornano (BS) was improved by applying suitable SbMD, SbPD and circularity strategies (S1 and S2, the latter being an adapted and upscaled version of the former). Environmentally, the three main impact drivers of the after-SSbD scenarios are the production of HNO_3 (main mass flow input), of $Zn(NO_3)_2$ (S1) or zinc powder (S2), and of electricity. Checking the single score, the reduction achieved in S1 and S2 with respect to BS was of 52 and 67 %, respectively, which confirmed the efficacy of the applied SSbD measures and, ultimately, of the scaled-up circular production of S2. This is also reflected in the economic assessment, since the production of 1 kg of Mn-doped ZnO nanopowder through S2 is roughly four times cheaper than that conducted *via* BS. Anyway, the main cost driver and hotspot in the two redesigned scenarios was the labour expense, accounting for more than 75 % of the total cost inputs. S-LCA also supports the suitability of the SSbD approaches, which led to a dramatic reduction of the social footprint of the complete product-system: around 48 % from BS to S1, and about 87 % from BS to S2. This responds to a more efficient use of the resources, which translates into more outputs to distribute the risks across. The uncertainty analysis carried out for the environmental, economic and social evaluation of each scenario do not impact the interpretation of results, and allowed to perform MCDA. The MCDA outcome confirmed that the upscaled process, S2, was the best-performing scenario from the sustainability viewpoint, with almost 100 % likelihood of being placed in the first position of the ranking among the three options, and S1 'winning' the silver of the classification; the performed sensitivity analysis demonstrated that this trend is maintained regardless of the weights assigned to the environmental, economic and social indicators. However, more research is needed to effectively communicate integrated results in a clear and actionable way, ensuring that they are ultimately useful for informed decision-making, without the risk of overlooking relevant impacts, and to extend the application of the presented methodologies to other industrial sectors. On the other hand, impacts attributable to ZnO NPs emissions, together with their characterisation factors, should be considered in the analyses. Calculation of both is however not trivial and time-consuming, but they are being investigated in our laboratories and the results will be presented in a future publication, also related to the 'Diagonal' project. In addition, it would be interesting to consider an expansion of the system boundaries, to include the use and end-of-life phases, when more data are available.

Altogether, the findings of this work highlight the potential of combining hybrid green synthetic methods with structured evaluation frameworks to support safety and holistic sustainability in industrial scenarios from the earliest stages of innovation. Scaling up processes like S2 to real-world settings will help validate their technical, socio-economic and environmental feasibility. Based on these findings, several recommendations can be made: for stakeholders in industry, the SSbD framework can support the adoption of sustainable processes like S1 and S2, aiming to reduce environmental impacts and production costs, while promoting circular economy strategies and social well-being. Finally, policy-makers should consider developing standardised guidelines for evaluating economic and social dimensions within the SSbD framework and incentivise the adoption of circular production methods.

CRediT authorship contribution statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.spc.2025.03.003.

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