An environmental study on starch aerogel for drug delivery applications: effect of plant scale-up

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Purpose The aim of this work is the evaluation and minimization, using a life cycle assessment approach, of the environmental impacts of starch aerogel production on different scale plants. Aerogels are porous structures, which can be used as carriers for delivery systems; they are obtained through a supercritical drying. The impacts related to the production of 1 g of starch aerogel on two different scales (vessel internal volumes equal to 0.5 L and 5.2 L) were evaluated and compared. The environmental impacts on an industrial scale plant were also simulated.

Methods All the quantities related to materials, energy consumption and emissions to air, soil and water were reported to the chosen functional unit (1 g of starch aerogel obtained on bench or pilot scale plant). Data were analysed using SimaPro 8.0.5 software, whereas the Ecoinvent 3.1 database and primary data were used for the life cycle inventory, according to the reference standard for LCA (i.e., ISO 14040-14044). A detailed analysis, following a gate-to-gate approach to quantify the emissions at plant level, which are generalizable for all polysaccharides' aerogel productions, was performed.In order to complete the study, the results of a cradle-to-gate analysis, quantifying the emissions at overall level, which are complete but related only to corn starch aerogel production, were also proposed. The IMPACT 2002+ method was used to evaluate the effect of the production on the midpoint and damage impact categories.

Results and discussion Scaling-up the starch aerogel production from bench to pilot scale induced a substantial reduction of the impacts on all the categories. On both scales, the analysis made using midpoint categories showed that supercritical drying step strongly affected carcinogens and mineral extraction, whereas alcogel production step strongly affected respiratory organics. Solutions aimed at minimizing these impacts were proposed. The performed analysis, using both midpoint and endpoint categories, allowed to identify the aerogel production weak points and propose improved solutions.

Conclusions Global emissions related to starch aerogel production were lowered passing from bench scale to pilot scale. By using damage categories, it was possible to quantify a global reduction of 40 % of the emissions on human health, climate change, ecosystem quality and resources. The simulation on industrial scale led to a total reduction of 82 % of the damage with respect to pilot scale plant and of 95 % with respect to bench scale plant.

Keywords: Life cycle assessment, starch aerogel, plant scale-up, process optimization, drug delivery system, sustainability.

1 Introduction

Drug delivery systems (DDS) are either lipid- or polymer-based nanoparticles or microparticles properly designed to improve the pharmacological and therapeutic properties of parenterally administered drugs (Allen and Cullis 2004) or to increase the poorly water-soluble drugs dissolution rate (Dahan and Hoffman 2008). Therefore, different techniques were proposed, including micronization, solid dispersion and inclusion complexation, in order to obtain targeted mean diameter and size distribution microparticles with improved drug dissolution rate (Gómez-Galván et al. 2016; Prosapio et al. 2015; Saffari et al. 2016). A possible alternative to the use of size-reduction techniques is based on the dispersion of the drug on a biocompatible and, if possible, biodegradable porous substrate (Mehling et al. 2009). Different kinds of porous substrates can be used for this purpose, such as, for example, membranes (Thombre et al. 1999), metal-organic matrices (Horcajada et al. 2008) or structures with functionalized surfaces (Zhao et al. 2011).

Due to high porosities, open pore structures, and large surface areas, nanostructured aerogels represent a promising class of materials to be used as carriers for DDS (Ulker and Erkey 2014). Silica aerogels, showing outstanding properties in terms of porosity (90–99 %) and surface areas (400–1000 m^2/g), are frequently used as host matrices for oral delivery systems (Caputo et al. 2012; Smirnova et al. 2004). Nevertheless, these aerogels are biocompatible and, therefore, not toxic for human body, but not biodegradable and, therefore, they cannot be enzymatically decomposed in the human body (Smirnova et al. 2003).

An alternative to silica aerogels may be the use of natural polysaccharides based aerogels, such as starch, alginate or chitosan, because of their low toxicity, renewability and stability (Baldino et al. 2015; García-González et al. 2011). Those aerogels may be obtained from wet gels by using a supercritical drying process, suitable to avoid the pore collapse phenomenon, keeping intact the porous structure of the wet material (Cardea et al. 2013). Among polysaccharides, starch is available in great quantities at low costs and is used in DDS in form of microspheres (Malafaya et al. 2006) or in form of aerogels (García-González and Smirnova 2013). In a previous work, the effect of process parameters (such as solvent exchanging time and starch concentration) on the morphology of starch aerogels produced from different sources (corn, potato and wheat) was evaluated. De Marco et al. identified the best operating conditions in order to obtain nanostructured porous aerogels: starch obtained from corn with a starting concentration in water equal to 15 %, using 24 h for each water-ethyl alcohol exchange (De Marco et al. 2015a). The capability of polysaccharides based aerogels to be used as carriers for drugs (García-González et al. 2011) or vitamins (De Marco and Reverchon 2017; Pantić et al. 2016) was also proved.

1.1 LCA literature review

Even though polysaccharides based aerogels may be classified as eco-friendly materials due to their biodegradability, their production requires organic solvent usage and high-pressure vessels running for many hours. The environmental aspects associated with a specific production may be quantified using a Life Cycle Assessment (LCA) approach (Finnveden et al. 2009).

Indeed, in the last years, several LCA studies were performed in different fields, such as, for example, energy (González-García et al. 2014; Lardon et al. 2009; Lijó et al. 2015; Pehnt 2006), healthcare (De Soete et al. 2014; Jiménez-González et al. 2004; Landry and Boyer 2016; McAlister et al. 2016; Wernet et al. 2010), food (De Marco and Iannone 2017; De Marco et al. 2015b), and wines (Gazulla et al. 2010; Iannone et al. 2014; Iannone et al. 2016),.

LCA healthcare studies concerning the synthesis of the pharmaceutical principle are rarely publicly available (Sherman et al. 2012) and, even when data are published, in some cases, for confidential reasons, the name of the active pharmaceutical ingredient (API) is not provided. For example, Wernet et al. carried out a “cradle-to-factory gate” LCA of the production of a pharmaceutical principle, without indicating its name (Wernet et al. 2010), whereas Jiménez-González et al. identified and analyzed the “cradle-to-gate” environmental impacts of a typical API synthesis, focusing the attention in the optimization of the solvent use with the aim of reducing the impacts (Jiménez-González et al. 2004). Lack of life cycle inventory data leads to difficulties in studying the emissions of specific or very innovative products (Burgess and Brennan 2001). Aerogel production falls under this category, because it is difficult to source data in literature.

In particular, a “from cradle to factory gate” LCA study on transparent silica aerogel, obtained using low and high temperature supercritical drying (LTSCD and HTSCD), which can be used as translucent insulation material, was performed using primary data (Dowson et al. 2012). In that study, the supercritical drying operation was conducted on an autoclave with an internal volume of 1 L. For both LTSCD and HTSCD processes, the total energy use and carbon dioxide burden were determined and scaled up to produce a 1 m^3 volume of aerogel.

De Marco et al. used primary data to preliminarily analyze life cycle emissions due to a three-steps starch aerogel production (De Marco et al. 2016). In the first step, a hydrogel was prepared using an aqueous solution; then, an alcogel was prepared by replacing the water contained in the hydrogel with ethyl alcohol; finally, a supercritical carbon dioxide drying was conducted on a bench scale high-pressure vessel with an internal volume of 80 mL.

1.2 Aim of the work

Literature related to pharmaceutical products’ and aerogel production LCA studies has been limited to few papers; in particular, a study on polysaccharides based aerogels produced on a pilot or an industrial scale has not yet been performed. Therefore, in order to determine the environmental impacts of new potential DDS, the aim of this study is the evaluation of the environmental impacts of starch aerogel production, considering the scale-up of the process. Both detailed “gate-to-gate” and “cradle-to-gate” analyses are proposed. Indeed, the impacts related to the production of 1 g of starch aerogel experimentally produced on two scales’ plants are compared using a “gate-to-gate” approach: bench scale (internal volume, V, of 0.5 L) and pilot scale (V = 5.2 L). This study identifies components of aerogel production on bench and pilot scale with the highest proportion of environmental emissions. Using interventions based on those emissions, we also model production on an industrial scale, considering both “gate-to-gate” and “cradle-to-gate” system boundaries. In this modelling, the internal volume of the vessel is equal to 100 L, which is a standard for pharmaceutical productions.

2 Materials and methods

2.1 Materials

In order to manufacture the starch aerogel, the following materials were purchased: corn starch from Fluka (Italy), ethanol (EtOH, purity 99.5 %) from Sigma-Aldrich (Italy), carbon dioxide (CO_2, purity 99.998) from Morlando group (Italy). All the products were used without further purifications. Water was distilled using a laboratory water distiller supplied by ISECO S.P.A. (St. Marcel, AO, Italy).

2.2 Aerogel preparation

In Table 1, the main activities of the process under observation are reported. Aerogel processing can be distinguished in three steps, as represented in Figure 1a where the IDEF (Icam DEF for Function Modelling) diagram is reported. Stages 1 and 2 are related to the agricultural processes of obtaining corn (stage 1) and extracting the starch from the corn (stage 2). In the subsequent stages, starch aerogel is obtained from starch.

First, the formation of starch hydrogel, starting from granules, occurs through gelatinization and retrogradation stages. The material is melted in an aqueous medium to induce changes in the structure caused by breaking down the intermolecular bonds of starch molecules in the presence of water and heat; this cooked starch rearranges itself again to a more crystalline structure during a cooling step.

During gelatinization (stage 3 in Figure 1a), the corn starch is dissolved in distilled water (with a concentration of 15 % wt); the obtained solution is stirred at 75 °C for 24 h until it becomes homogeneous. The solution, called cooked starch, is put into cylindrical moulds with a height of 1 cm: in the case of the samples to be treated in the bench plant, the internal diameter of the moulds is 2 cm, whereas, in the case of the samples to be treated in the pilot plant, the internal diameter is 6 cm. Then, the samples are placed in the refrigerator for retrogradation at 4 °C for three days (stage 4 in Figure 1a) resulting in the formation of hydrogel.

The following step is the alcogel formation (stage 5 in Figure 1a), obtained by substituting the water filling the hydrogel pores with EtOH at room temperature. This substitution is gradual and happens by batch equilibration with a succession of ethanol baths at increasing ethanol concentrations (40 %, 70 %, 90 % and 100 % (v/v)) (Glenn and Stern 1999). Each ethanol bath contains two volumes of liquid for each volume of gel and the equilibration time for each bath is 24 h.

The last step in the formation of aerogel is the supercritical drying of the alcogel, shown in Figure 1b. The apparatus used in our lab is diagrammed in Figure 2. In an experimental test, the alcogel samples are placed in the vessel (0.5 L for the bench-scale and 5.2 L for the pilot-scale), which is the core of the apparatus; the vessel is closed and, through a high-pressure pump, is filled from the top with supercritical carbon dioxide (sc-CO_2) (stage 6.1 in Figure 1b). Carbon dioxide is cooled in a refrigerating bath, before pumping, to avoid cavitation. When the desired pressure (20 MPa) and temperature (45 °C) are reached (stage 6.2 in Figure 1b), drying is performed (stage 6.3 in Figure 1b). A test gauge manometer measures the pressure in the vessel, which, then, is regulated by a micrometering valve. A proportional-integral-derivative controller, connected with electrically controlled thin bands, sets the temperature. The sc-CO_2 flow rate is fixed at 2 kg/h in the case of bench scale and at 20 kg/h in the case of pilot scale plant; the corresponding residence time inside the vessel is about 4 min. A rotameter and a dry test meter measures CO_2 flow rate and the total quantity of CO_2 delivered, respectively. After drying of 5 hours, a slow depressurization (20 min) brings the system back to atmospheric pressure (stage 6.4 in Figure 1b); the aerogel can be recovered from the vessel.

Starting from the experimental results obtained on both bench and pilot scale, a simulation of an industrial plant with a vessel of 100 L is also performed. Different from bench and pilot scale plants, in the industrial simulation, the heating of the vessel is done with a heating jacket using vapor at 150 °C and 1 bar; the vapor is produced in a burner using methane as fuel. The carbon dioxide is recycled after condensation in a horizontal exchanger with a square pitch and 4 tube passes. The cooling process is conducted with water at 5 °C, instead. These choices are made considering the hot and cold utilities typically used in supercritical fluids based industrial scale plants. Other differences between bench and pilot scale and the assumptions made to simulate the industrial scale plant are reported in Table 2.

3 LCA methodology

3.1 Goal definition, functional unit and system boundaries

The purpose of this study is the evaluation of the environmental impacts of corn starch aerogel production at different production scales, in order to understand how much the plant scale-up influences the environmental emissions. The chosen functional unit (FU) is 1 g of final aerogel, considering that the production of a specific quantity of aerogel obtained through the supercritical drying is independent on the material constituting the aerogel. It means that the results obtained in this work can be generalized for all the natural polysaccharides based aerogels.

For quantification at plant level (gate-to-gate), mass and energy balances of each operation were performed; therefore, the system boundaries of the detailed analysis, constituting the foreground system of this work, can be identified in Figure 1a (dashed line) and are set from starch powder transportation to aerogel production. The results obtained in this way are valid also for other polysaccharides based aerogels, if they are produced through hydrogel formation, alcogel formation and supercritical drying. In the final part of the paper, data related to the emissions at overall level (cradle-to-gate), which are complete but related only to corn starch aerogel production, were also supplied; in this case, the background system is included in the analysis and the boundaries are set from corn cultivation to aerogel production (continuous line in Figure 1a).

3.2 Life cycle inventory

In order to compile the Life Cycle Inventory (LCI), measured data regarding materials, water and the amount of electricity used during each step of the process were collected directly from the production site. Other background data, such as inputs and outputs associated with the production of 1 kWh of electricity or tap water related to the utilities servicing the plants, were recovered from the internationally recognized source Ecoinvent 3.1. In our study, according to ISO 14040-14044 (the reference standard for LCA), which recommend to avoid allocation, single processes producing single outputs were considered.

For each step of the bench and pilot-scale process, input data (mainly energy, water and materials) and output data (emission to air, water and soil) were collected. In Table 3, the main inputs and outputs constituting the LCI for starch aerogel production (referred to the functional unit) are listed. The simulation on industrial scale was performed considering the typical choices that are made when pharmaceutical plants using supercritical fluids based processes are designed. This LCA study, according with ISO 14040-14044 (the reference standard for LCA), was conducted using the LCA software SimaPro 8.0.5.

3.3 Impact category selection

In this paper, the IMPACT 2002+ method was used to evaluate the contributions of different stages of the process. This method was selected because the study pertains to a European (Italian) production and IMPACT 2002+ was developed in Europe by the Swiss Federal Institute of Technology Lausanne (EPFL), Switzerland. Using this methodology, all types of LCI results (elementary flows and other interventions) are linked via several midpoint categories to endpoint (or damage) categories. According to this methodology, the midpoint categories allowing the classification and characterization of the environmental impacts are: human toxicity carcinogenic effects (C), human toxicity non-carcinogenic effects (NC), respiratory effects due to inorganics (RI), ionizing radiation (IR), ozone layer depletion (OLD), photochemical oxidation due to respiratory organics (RO), aquatic ecotoxicity (AET), terrestrial ecotoxicity (TET), aquatic acidification (AA), aquatic eutrophication (AE), terrestrial acidification/nitrification (TAN), land occupation (LO), global warming potential (GWP), non-renewable energy consumption (NRE) and mineral extraction (ME). All midpoint scores are related to the four damage categories: human health, ecosystem quality, climate change, and resources (Jolliet et al. 2003).

4 Results and discussion

4.1 Environmental IMPACT 2002+ analysis: characterization and normalized characterization categories at midpoint and endpoint level

The aim of this study is the environmental analysis of the production of starch aerogel on different scales. Table 4 shows the IMPACT 2002+ midpoint results for aerogel production on bench scale and on pilot scale, considering a from "gate-to-gate" approach. In particular, the percentages reported in the fifth column of Table 4 highlight the reduction of emissions using the pilot-scale plant instead of the bench-scale plant.

The aerogel production is based on a three-step process: gelatinization (stage 3 in Figure 1) and retrogradation (stage 4) to obtain hydrogel, ethanol substitution to obtain alcogel (stage 5) and supercritical drying to obtain aerogel (stage 6). Figure 3 reports the relative contributions of each phase on the midpoint characterization categories for bench scale (boxes on the left) and pilot scale plant (boxes on the right). It is possible to observe that, on both scales, the category of respiratory organics is strongly influenced by the alcogel formation step (stage 5); i.e., when the organic solvent (ethanol) substitutes water in the hydrogel. Considering the other categories, there is a marked difference between the bench- and pilot-scales in the relative environmental emissions from each stage of production, as shown in Figure 3.

On bench scale, OLD is mainly influenced by the hydrogel formation (stages 3 and 4), some categories (such as C, NC, RI, AET, AA, AE and ME) are primarily influenced by the supercritical drying step (stage 6), and for the remaining categories (IR, TET, TAN, LO, GWP and NRE), the effect of the hydrogel formation and the supercritical drying to obtain the aerogel is comparable.

On the pilot scale, the highest contributor for all categories except for respiratory organics is due to step 6, where alcogel is dried by supercritical carbon dioxide to form an aerogel. This is expected as the majority of energy consumption occurs during this step.

In order to compare the different impact categories, the emissions were normalized. In Table 5, the normalization midpoint categories factors and the normalized midpoint categories for both the bench-scale and pilot-scale productions are reported. After the normalization, it was possible to select the midpoint categories mainly affected by each step of the process, and propose process modifications aimed at reducing the emissions. It is evident that, both on bench and on pilot scale, the midpoint categories mainly affected by the process under study are carcinogens, respiratory organics, and mineral extraction.

The large carcinogens impact is mainly due to the high quantity of carbon dioxide used in the supercritical drying step (considering the bench scale plant, the 78 % of the carcinogens obtained in the drying step is due to carbon dioxide, the remaining 22 % is due to electricity usage). A substantial reduction of these emissions could be obtained by condensing and recycling the carbon dioxide after its usage, as is commonly done in industrial scale plants.

The impact on respiratory organics is due to alcogel formation (stage 5) because of the organic solvent used in this step (shown in Figure 3). It is possible to reduce the quantity of ethanol used, considering an alternative to the actual process, as demonstrated by García-González and Smirnova (García-González and Smirnova 2013). Indeed, it is possible to obtain the formation of alcogel starting from hydrogel using two subsequent ethanol-water baths, instead of four; in this case, the exchanging times will be 48 hours and the subsequent baths will be prepared at ethanol concentrations of 40 % and 100 %.

The third largest emissions category is mineral extraction, linked with the use of energy mainly in the aerogel formation step (stage 6 in Figure 1). Considering that some process variables cannot be altered (such as, for example, process pressure and temperature), a “lowering emissions” solution can consist in the substitution of part of the electricity with alternative forms of energy (Fera et al. 2014), in the reduction of the drying time or in a reduction of carbon dioxide flow rate.

According to IMPACT 2002+ method, the impacts at midpoint level were linked to damage categories (Jolliet et al. 2003).

The four global environmental impact categories at endpoint level are shown in Figure 4 for bench and pilot scale plants. Observing the figure, it is evident that, for each of the damage categories, the impact due to the production on bench scale is much higher than the one on pilot scale.

In particular, there is a reduction of the environmental impact of 68 % considering the human health, 72 % considering both ecosystem quality and climate change and 74 % considering the resources.

4.2 Improved solution: midpoint and damage categories

Using results obtained on bench and pilot scale aerogel production, we proposed improvements to be used on the industrial scale to minimize the impact. These include:

a) alcogel formation using a two-step process instead of a four-step process;
b) condensation and recycling of carbon dioxide used in drying operation;
c) drying time equal to four hours instead of five hours.

In order to verify that these process modifications (a, b, and c) do not alter the characteristics of the aerogel, which has to be nanostructured and porous to be used as carrier for DDS, a sample was prepared in the following way: alcogel was prepared according to the hypothesis a) and was processed on the bench scale plant, modifying the operating conditions in agreement with the hypothesis c). A microscopy analysis revealed that the aerogel obtained in the improved solution conditions preserved the nanostructured morphology obtained in the base case. Moreover, a nitrogen adsorption and desorption test revealed that the surface area, key parameter in the case of porous materials, was unaltered with respect to the aerogel obtained in the base case operating conditions.

Once assured that the aerogel obtained using the improved solution conditions a) and c) was appropriate to be used as carrier for DDS, a simulation on an industrial plant was performed, considering also hypothesis b). The assumptions made in the project of the industrial plant were reported in the last column of Table 2, considering the choices made on different existing plants using supercritical fluids based technologies. In the last column of Table 3, the inventory of the aerogel production on industrial scale was reported, and the corresponding IMPACT 2002+ midpoint results were reported in the sixth column of Table 4; the reduction of the emissions obtained using the industrial plant with respect to bench and pilot plant was highlighted in the last two columns of Table 4. Observing the values shown in Table 4, it is evident that the industrial scale is recommended not only from the economical point of view, but also from the environmental point of view. Indeed, passing from bench to industrial scale, there was a reduction in emissions larger than 90 % for all midpoint categories except respiratory organics. This evidence can be explained by the choices a), b) and c) related the improved solution and considering that the individual processes' efficiency on industrial scale is higher than the other scales, due to the optimization made in order to minimize the waste of resources. Finally, the emissions at endpoint level and the global environmental savings were shown in Table 6.

In order to complete the analysis, a comparison among the emissions, at endpoint level, related to the gate-to-gate production and the cradle-to-gate production was performed. In this way, it was possible to compare the emissions of the agricultural stages with the emissions of the industrial stages of the process. Figure 5 clearly showed the contribution of the gate-to-gate process (industrial steps) with respect to the cradle-to-gate production (agricultural + industrial steps). It is evident that the contribution of the agricultural stages to obtain the corn and of the production of starch starting from corn had considerable impacts on ecosystem quality. On the contrary, the impacts on human health, climate change and resources were mainly due to the industrial stages of the process.

5 Conclusions and perspectives

In this study, we performed a LCA analysis regarding the production on different scales of aerogel, which can be used as carrier for drug delivery. We observed that the midpoint categories mainly affected by the process are carcinogens, respiratory organics and mineral extraction and, on all of them, the emissions were lowered passing from bench scale to pilot scale. It was possible to quantify a total reduction of 40 % of the emissions in terms of human health, climate change, ecosystem quality and resources if the process is conducted on pilot-scale rather than on bench-scale. An improved solution, aimed at reducing the emissions, was proposed and, once verified that the aerogel obtained in these conditions is suitable to be used as carrier for drug delivery, a simulation on industrial scale (with a vessel volume of the dryer typical, in the case of pharmaceutical industries using supercritical fluids based processes) was performed. In this case, a global reduction of 82 % of the damage with respect to pilot scale plant and of 95 % with respect to bench scale plant was detected. The results obtained in this gate-to-gate analysis are valid also for other aerogels obtainable using the same production process. Finally, we compared the emissions of the gate-to-gate process with the ones of a cradle-to-gate process, observing that the cultivation of corn and its transformation in starch had a significant effect only on ecosystem quality.

Further studies regarding the LCA analysis of pharmaceutical principles adsorbed on starch aerogel or on similar supports will be performed, considering the emissions related to the drug synthesis and drug processing.

List of abbreviations

AA: aquatic acidification;

AE: aquatic eutrophication;

AET: aquatic ecotoxicity;

C: carcinogens;

DALY: disability adjusted life years;

DD: drum drying based technique;

FU: functional unit;

GWP: global warming potential;

ICAM: integrated computer aided manufacturing;

IDEF: Icam def for function modelling;

IR: ionizing radiations;

LCA: life cycle assessment;

LCI: life cycle inventory;

LO: land occupation;

MD: multistage drying based technique;

ME: mineral extraction;

NC: non-carcinogens;

NRE: non-renewable energy consumption;

OLD: ozone layer depletion;

PDF: potentially disappeared fraction of species;

RI: respiratory inorganics;

RO: respiratory organics;

TAN: terrestrial acidification/nitrification;

TET: terrestrial ecotoxicity.

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Table 1: Process details and assumptions. For each step, the corresponding phase reported in Figure 2a and b is indicated in brackets.

Process	Characteristics and details
Energy supply to facility	Italian energy mix low voltage
Gelatinization step (3)	T=75 °C; t=24 h; energy and water supply
Retrogradation step (4)	T=4 °C; t=72 h; energy supply for cooling
Alcogel formation (5)	T=25 °C; t=96 h; ethanol and water supply; energy supply
Pressurization (6.1)	t=0.08 h; carbon dioxide supply; energy supply
Operating conditions’ stabilization (6.2)	T=45 °C; P=200 bar; t=0.25 h; carbon dioxide supply; energy supply
Drying (6.3)	T=45 °C; P=200 bar; t=5 h; carbon dioxide supply; energy supply
Depressurization (6.4)	T=25 °C; P=1 bar; t=0.33 h

Table 2: Bench and pilot plant specifications; assumption made on the industrial scale simulation.

Process	Bench scale	Pilot scale	Industrial scale simulation
CO_2 flow rate, kg/h	2	20	440
Vessel volume, L	0.5	5.2	100
Height to diameter ratio	9.4	9.4	9.4
Sample diameter, m	0.02	0.06	0.2
Sample number	4	8	22
Hot utility	Electrical heater bands	Electrical heater bands	Vapour at 150 °C and 1 bar
Cold utility	Refrigerating bath	Refrigerating bath	Cooling water at 5 °C

Table 3: Life cycle inventory of the main inputs and outputs for starch aerogel production.

Production Phase	Input/Output	Unit	Bench plant	Pilot plant	Industrial plant
Gelatinization step	Starch	g	6.54E-01	6.54E-01	6.54E-01
	Water	g	3.71E+00	3.71E+00	3.71E+00
	Electricity	kJ	9.90E+03	5.50E+02	1.98E+01
Retrogradation step	Hydrogel	g	4.36E+00	4.36E+00	4.36E+00
	Electricity for cooling	kJ	1.18E+03	6.58E+01	2.37E+00
Alcogel 40 %	Hydrogel	g	4.36E+00	4.36E+00	4.36E+00
	Ethanol	g	3.45E+00	3.45E+00	3.45E+00
	Water	g	6.55E+00	6.55E+00	6.55E+00
	Output				
	Ethanol	g	2.69E+00	2.69E+00	2.69E+00
	Water	g	8.82E+00	8.82E+00	8.82E+00
Alcogel 70 %	Alcogel 40 %	g	2.84E+00	2.84E+00	
	Ethanol	g	6.03E+00	6.03E+00	
	Water	g	3.27E+00	3.27E+00	
	Output				
	Ethanol	g	5.20E+00	5.20E+00	
	Water	g	5.01E+00	5.01E+00	
Alcogel 90 %	Alcogel 70 %	g	1.94E+00	1.94E+00	
	Ethanol	g	7.76E+00	7.76E+00	
	Water	g	1.09E+00	1.09E+00	
	Output				
	Ethanol	g	6.82E+00	6.82E+00	
	Water	g	2.24E+00	2.24E+00	
Alcogel 100 %	Alcogel 90 %	g	1.73E+00	1.73E+00	2.84E+00
	Ethanol	g	8.62E+00	8.62E+00	1.09E+01
	Output				
	Ethanol	g	7.75E+00	7.75E+00	7.34E+00
	Water	g	1.07E+00	1.07E+00	2.18E+00
Drying	Alcogel 100 %	g	1.52E+00	1.52E+00	1.94E+00
	Carbon dioxide	g	2.13E+03	1.19E+03	6.93E+01
	Electricity	kJ	3.04E+03	8.28E+02	6.60E+01
	Electricity for cooling	kJ	5.59E+02	1.78E+02	2.61E+01
	Output				
	Aerogel	g	1.00E+00	1.00E+00	1.00E+00
	Carbon dioxide	g	2.13E+03	1.19E+03	6.93E+01
	Ethanol	g	5.18E-01	5.18E-01	9.36E-01

Table 4: IMPACT 2002+ midpoint results for starch aerogel production per FU (1 g of aerogel produced on a lab or a pilot plant).

Midpoint category	Unit	Bench scale	Pilot scale	Changes in impact from bench to pilot	Industrial scale simulation	Changes in impact from bench to industrial	Changes in impact from pilot to industrial
C	kg C_2H_3Cl eq	9.86E-02	3.31E-02	-67 %	5.63E-03	-94 %	-83 %
NC	kg C_2H_3Cl eq	4.14E-02	1.56E-02	-62 %	1.72E-03	-96 %	-89 %
RI	kg PM2.5 eq	2.96E-03	9.26E-04	-69 %	1.29E-04	-96 %	-86 %
IR	Bq C-14 eq	6.37E+01	1.69E+01	-74 %	2.63E+00	-96 %	-84 %
OLD	kg CFC-11 eq	3.77E-07	7.03E-08	-81 %	1.64E-08	-96 %	-77 %
RO	kg C_2H_4 eq	9.93E-03	8.14E-03	-18 %	6.86E-03	-31 %	-16 %
AET	kg TEG water	2.17E+02	6.53E+01	-70 %	9.41E+00	-96 %	-86 %
TET	kg TEG soil	5.67E+01	1.58E+01	-72 %	2.43E+00	-96 %	-85 %
TAN	kg SO_2 eq	5.09E-02	1.44E-02	-72 %	2.34E-03	-95 %	-84 %
LO	m^2 org.arable	4.26E-02	1.16E-02	-73 %	1.86E-03	-96 %	-84 %
AA	kg SO_2 eq	1.78E-02	5.25E-03	-71 %	7.91E-04	-96 %	-85 %
AE	kg PO_4 P-lim	6.77E-04	2.63E-04	-61 %	4.71E-05	-93 %	-82 %
GWP	kg CO_2 eq	3.84E+00	1.06E+00	-735 %	1.75E-01	-95 %	-84 %
NRE	MJ primary	6.14E+01	1.59E+01	-74 %	3.36E+00	-95 %	-79 %
ME	MJ surplus	2.09E-01	8.36E-02	-60 %	8.47E-03	-96 %	-90 %

C: carcinogens, NC: Non Carcinogens, RI: Respiratory inorganics, IR: Ionizing radiation, OLD: Ozone layer depletion, RO: Respiratory organics, AET: Aquatic ecotoxicity, TET: Terrestrial ecotoxicity, TAN: Terrestrial acidification/nitrification, LO: Land occupation, AA: Aquatic acidification, AE: Aquatic eutrophication, GWP: Global warming potential, NRE: Non-renewable energy, ME: Mineral extraction.

Table 5: Normalization factors and normalized impact categories at midpoint level for the bench-scale and pilot-scale aerogel production per FU (1 g of aerogel).

Midpoint category	Normalization factors	Bench scale	Pilot scale
C	4.55E+01	2.17E-03	7.27E-04
NC	1.73E+02	2.39E-04	9.02E-05
RI	8.80E+00	3.36E-04	1.05E-04
IR	5.33E+05	1.20E-04	3.17E-05
OLD	2.04E-01	1.85E-06	3.45E-07
RO	1.24E+01	8.01E-04	6.56E-04
AET	1.36E+06	1.60E-04	4.80E-05
TET	1.20E+06	4.73E-05	1.32E-05
TAN	3.15E+02	1.62E-04	4.57E-05
LO	3.46E+03	1.23E-05	3.35E-06
AA	6.62E+01	2.69E-04	7.93E-05
AE	1.18E+01	5.74E-05	2.23E-05
GWP	9.95E+03	3.86E-04	1.07E-04
NRE	1.52E+05	4.04E-04	1.05E-04
ME	2.92E+02	7.16E-04	2.86E-04

C: carcinogens, NC: Non Carcinogens, RI: Respiratory inorganics, IR: Ionizing radiation, OLD: Ozone layer depletion, RO: Respiratory organics, AET: Aquatic ecotoxicity, TET: Terrestrial ecotoxicity, TAN: Terrestrial acidification/nitrification, LO: Land occupation, AA: Aquatic acidification, AE: Aquatic eutrophication, GWP: Global warming potential, NRE: Non-renewable energy, ME: Mineral extraction.

Table 6: IMPACT 2002+ damage results for starch aerogel production per FU (1 g of aerogel produced on all the tested and simulated scales).

Damage category	Unit	Bench plant	Pilot plant	Industrial plant	Impact reduction (compared to bench scale)	Impact reduction (compared to bench scale)
Human health	DALY	2.50E-06	8.09E-07	1.26E-07	-95 %	-84 %
Ecosystem quality	PDF·m^2·y	5.63E-01	1.57E-01	2.43E-02	-96 %	-85 %
Climate change	kg CO_2-eq	4.50E+00	1.24E+00	2.05E-01	-95 %	-84 %
Resources	MJ	6.16E+01	1.60E+01	3.37E+00	-95 %	-79 %

Figure captions

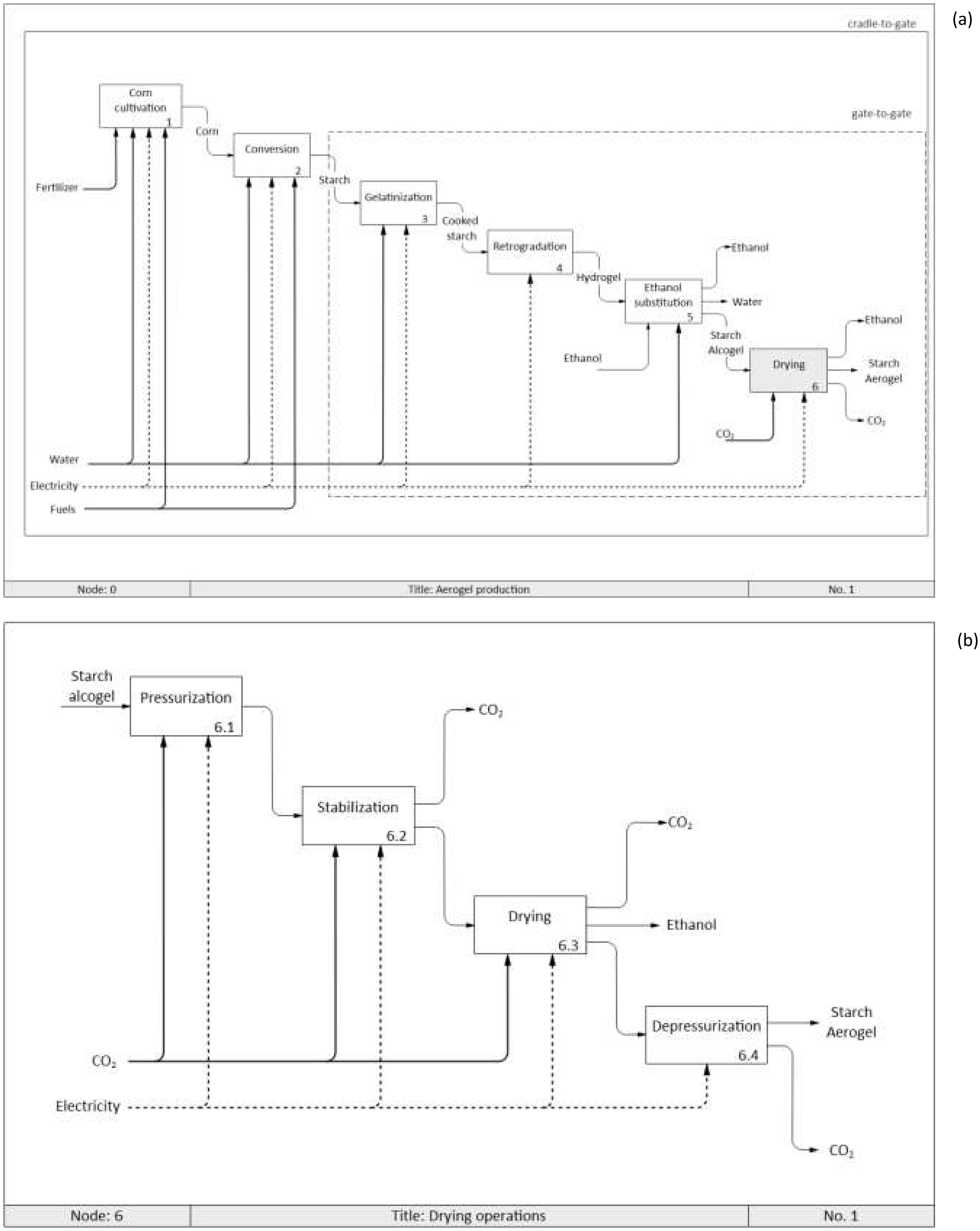
Fig. 1 IDEF diagrams of aerogel production for both bench and pilot scale; a) complete process scheme; b) details of drying operations.

Fig. 2 Sketch of the plant for aerogel's drying. CO_2: carbon dioxide supply; RB: refrigerating bath; P: pump; V: vessel; TC: thermocouple; M: manometer; PID: Proportional-Integral-Derivative controller; MV: micrometering valve; LS: liquid separator; BPV: back-pressure valve; R: rotameter and DM: dry test meter.

Fig. 3 Relative contributions of the three phases of starch aerogel production on bench scale and pilot scale plants. For each category, the box on the left is referred to the bench scale plant, the one on the right to the pilot scale plant. With reference to stages indicated in Figure 1, hydrogel corresponds to stages 3 and 4, alcogel to stage 5, and aerogel to stage 6.
C: carcinogens, NC: Non Carcinogens, RI: Respiratory inorganics, IR: Ionizing radiation, OLD: Ozone layer depletion, RO: Respiratory organics, AET: Aquatic ecotoxicity, TET: Terrestrial ecotoxicity, TAN: Terrestrial acidification/nitrification, LO: Land occupation, AA: Aquatic acidification, AE: Aquatic eutrophication, GWP: Global warming potential, NRE: Non-renewable energy, ME: Mineral extraction.

Fig. 4 Damage categories for aerogel production per FU.

Fig. 5 Emissions at endpoint level of a gate-to-gate and a cradle-to-gate aerogel production per FU.



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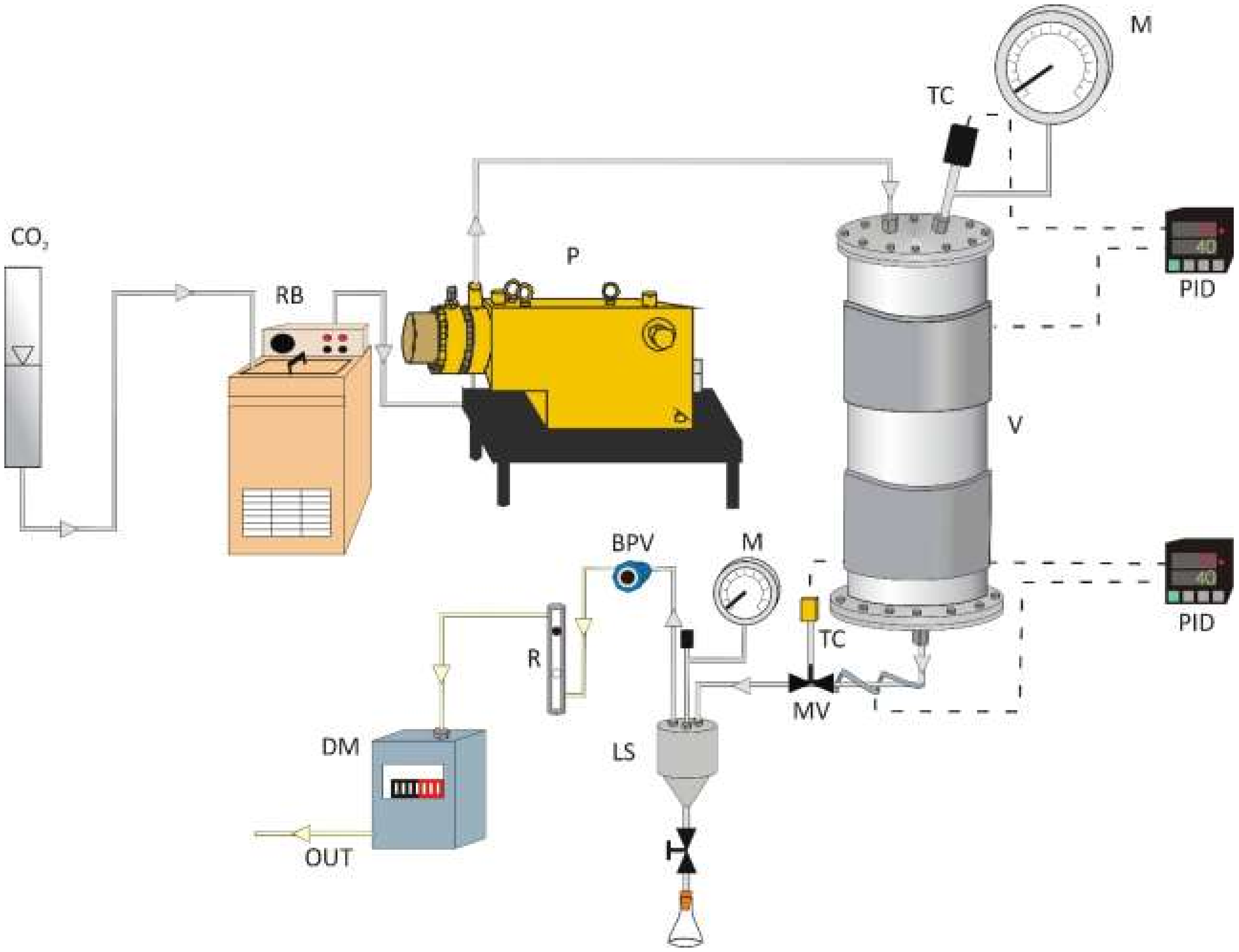

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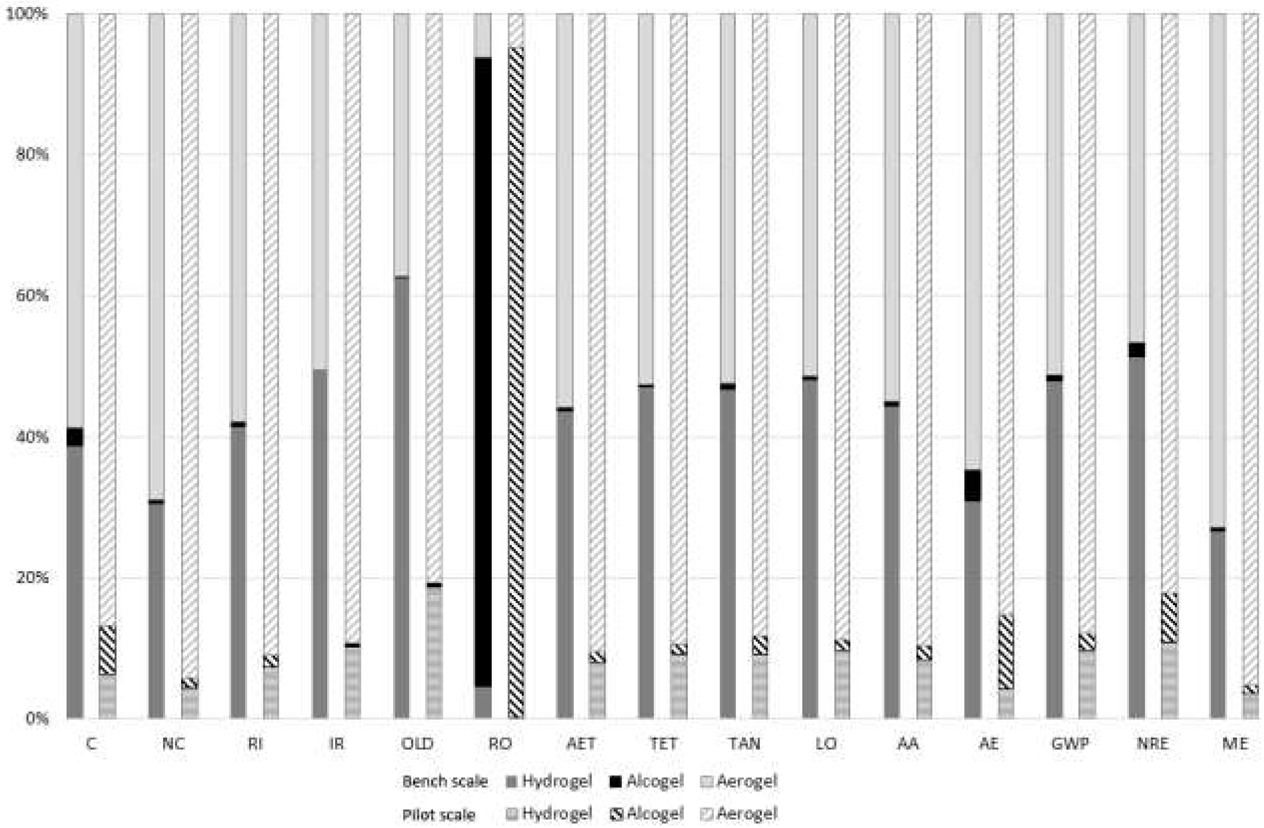

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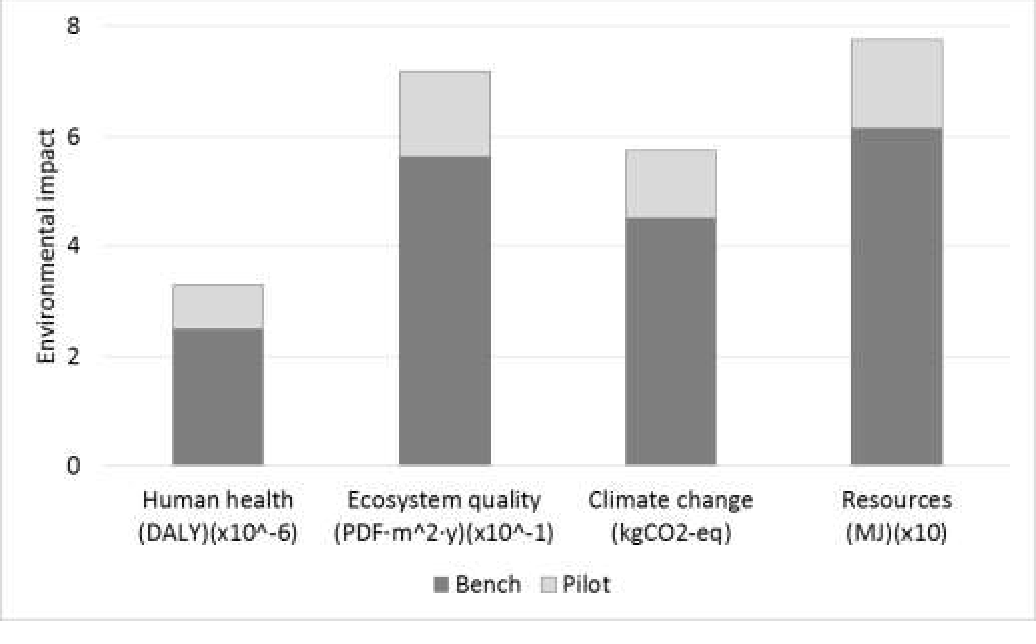

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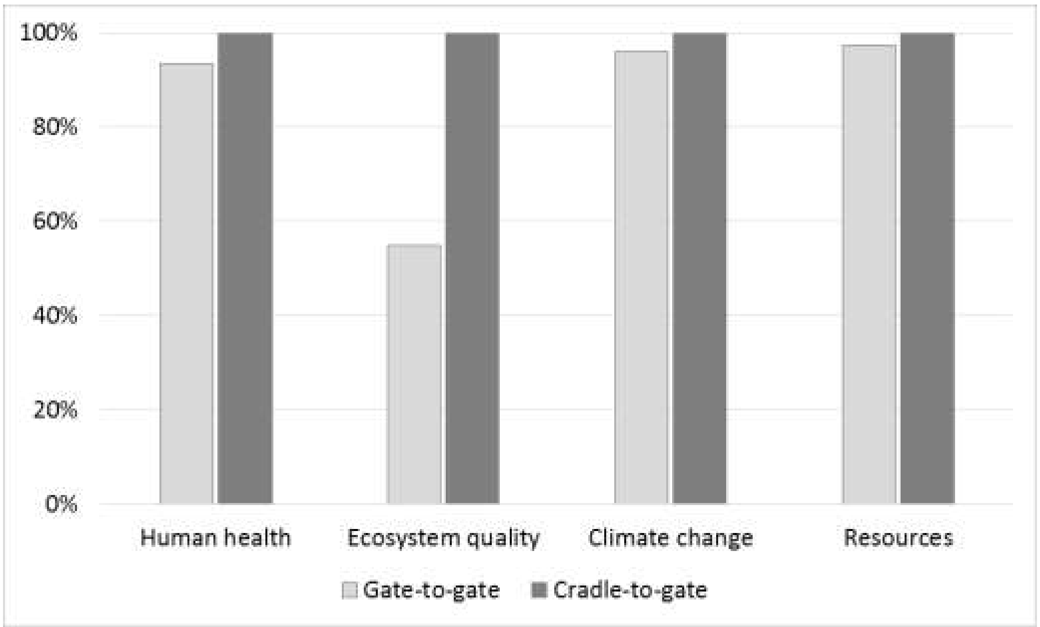

Fig. 5 Emissions at endpoint level of a gate-to-gate and a cradle-to-gate aerogel production per FU.