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LCA of Aerogel Production using Supercritical Gel Drying: from Bench Scale to Industrial Scale

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In the last years, many studies on Drug Delivery Systems (DDS) were performed with the aim of improving the dissolution rate of poorly water-soluble drugs. Nanostructured aerogels, characterized by open pore structures and high surface areas, were frequently used as substrates where drugs can be adsorbed. In particular, different researches focused their attention on polysaccharide aerogels, which are biodegradable and biocompatible and, therefore, are good candidates to support active substances in DDS. In this work, maize starch aerogels were produced on different scale plants using a three-step process: first, the gel was prepared using an aqueous solution, then water was replaced by ethanol forming an alcogel and finally, carbon dioxide at supercritical conditions was used as non-solvent to dry the alcogel and obtain the aerogel. An analysis aimed at evaluating and minimizing, using Life Cycle Assessment (LCA) methodology, the environmental impacts of aerogel production on five different scale plants was carried out. The impacts related to the production of 1 kg of starch aerogel on two different scales (vessel internal volumes, V, equal to 0.5 L and 5.2 L) were evaluated using primary data; moreover, a modelling of the emissions due to productions on industrial scales (V equal to 50, 100 and 200 L) was also performed. 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 “from gate to gate” approach was followed; therefore, the system boundaries were set from starch powder transportation to aerogel production. The IMPACT 2002+ method was used to evaluate the effect of the production on the midpoint and damage impact categories.

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, such as the attainment of microparticles with controlled mean diameter and size distribution or the dispersion of the drug on a biocompatible and, if possible, biodegradable porous substrate (Mehling et al., 2009). Due to high porosities, open pore structures, and large surface areas, nanostructured aerogels represent a promising class of porous materials to be used as carriers for DDS (Ulker and Erkey, 2014) or vitamin delivery systems (De Marco and Reverchon, 2017). Silica aerogels, because of their extraordinary 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. 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 (García-González et al., 2011) that can be obtained through a supercritical carbon dioxide based process. 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., 2015a). Considering that the production of aerogels requires organic solvent usage and high-pressure vessels running for many hours (Cardea et al., 2013), it is important to evaluate the environmental emissions associated with their production. The quantification of environmental emissions may be performed by using a Life Cycle Assessment (LCA) approach (Finnveden et al., 2009). An

LCA analysis may consider the entire process, according to a cradle-to grave approach (Reap et al., 2008) or a part of it (Iannone et al., 2014). Several LCA studies on different fields were performed, such as, for example, healthcare (Wernet et al., 2010), food (De Marco et al., 2015b), semi-finished foods (De Marco and Iannone, 2017) and wines (Iannone et al., 2016). Unfortunately, LCA studies regarding specific or very innovative productions turn out to be very difficult to be carried out, because of lack of databases (De Marco et al., 2015c). Aerogel production falls under this category because it is difficult to source data in literature. A cradle-to-factory gate LCA study on transparent silica aerogel, obtained using low and high temperature supercritical drying, which can be used as translucent insulation material, was performed using primary data (Dowson et al., 2012). De Marco et al. (2016) used primary data to make a preliminary evaluation of life cycle emissions due to a three-step starch aerogel production on bench scale. Subsequently, the same authors considered the scale-up of the process, identifying the most crucial phases from the environmental point of view and they proposed an improved solution, which can be used on industrial scale (De Marco et al., 2017). Considering that this process is energy intensive, a remarkable further reduction of the emissions can be obtained, adopting electricity produced in sustainable way (Fera et al., 2014). Considering that a limited number of papers on LCA of aerogel production useful to put on the market novel DDs was published, the aim of this study is to evaluate the environmental impacts of starch aerogel production, considering different industrial scales. Therefore, the impacts related to the production of 1 kg of starch aerogel on two different scales (V equal to 0.5 L and 5.2 L) were evaluated using primary data. An estimation of the impact of productions on industrial scale plants (V equal to 50, 100 and 200 L) was also performed.

2. Methodology

LCA analysis allows to correlate a broad set of data regarding the life-cycle of a product or a process in order to individuate the phases of the process that are critical from an environmental point of view. The main step of an LCA analysis are presented in the following sub-sections.

2.1 Goal definition, functional unit and system boundaries

Goal definition is one of the most important phases of the LCA methodology, because the choices made at this stage influence the entire study. The purpose of this study is the evaluation of the environmental impacts of maize starch aerogel production on different scale plants (two real and three simulated), in order to understand how much the plant scale-up influences the environmental emissions.
The functional unit (FU) is the reference to which all the inputs and outputs have to be related. Considering that the attainment of a specific quantity of aerogel obtained through the supercritical drying is independent on the material constituting the aerogel, the chosen functional unit is 1 kg of final aerogel obtained on different scales.
Through mass and energy balances of each operation, a gate-to-gate analysis was performed; therefore, the system boundaries (dashed line in Figure 1) are set from starch powder transportation to aerogel attainment.

2.2 Data collection

In Table 1, the main activities of the observed process are reported. The life cycle inventory (LCI) is one of the most effort-consuming step and consists on the activities related to the search, the collection, and interpretation of the data necessary for the environmental assessment of the observed system. Aerogel processing started with the gelatinization step, consisting in the preparation of the maize starch solution with concentration equal to 15 % wt in distilled water; using a magnetic stirrer, the solution was stirred at 75 °C for 24 h when it became homogeneous. Then, it was poured into cylindrical moulds with a height of 1 cm and an internal diameter varying from 2 to 28 cm, depending on the scale of the plant. Then, the samples were placed in the refrigerator for retrogradation at 4 °C for three days. The subsequent step was the attainment of the alcogel, replacing the water filling the pores of the gel structure by ethanol at room temperature. The water in the hydrogel was gradually replaced by ethanol by batch equilibration with a succession of two ethanol baths at increasing ethanol concentration (Glenn and Stern, 1999). The alcogels were, then, dried in homemade apparatuses constituted by stainless steel cylindrical high-pressure vessels, equipped with high-pressure pumps used to deliver the carbon dioxide (Prosapio et al., 2014). Details are reported in Table 2 both for experiments performed on bench and pilot scale and for the three simulations on industrial plants, indicated with Ind1, Ind2 and Ind3. Pressure in the vessel was measured by a manometer and regulated by a micrometering valve. Drying was conducted at 200 bar and 45 °C for four hours. A slow depressurization was used to bring back the system at atmospheric pressure and recover the aerogels from the vessel. In the case of the simulation on the industrial scale plants, carbon dioxide was condensed and recycled.

Table 1: Process details and assumptions

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

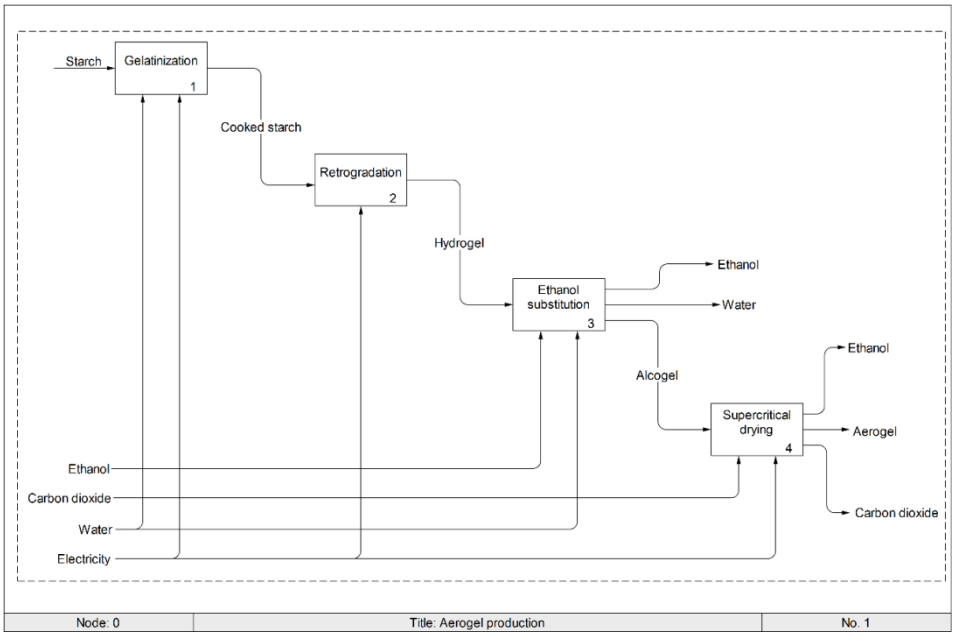

Figure 1: Aerogel production: scheme of the process and system boundaries.

2.3 Environmental analysis

The LCA study was conducted using the LCA software SimaPro 8.0.5. The majority of the processes and materials information were collected using "primary data", whereas Ecoinvent 3.1 database was employed for background data. Table 3 lists the inputs and outputs to produce 1 kg of starch aerogel on bench and pilot scale (real data) and on the industrial scales (simulated data). Once estimated the emissions related to the starch aerogel production through a LCI analysis, the corresponding environmental impacts have to be calculated using an LCA methodology. In this paper, the IMPACT 2002+ method was used to evaluate the contributions of different processes. This method was selected because the study pertains to a European (Italian) production and IMPACT 2002+ was one of the method developed in Europe.
This methodology proposed an implementation of a combined midpoint/endpoint approach, linking all types of LCI results (elementary flows and other interventions) via fifteen midpoint categories to four endpoint (or damage) categories. The fifteen midpoint categories 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). According to IMPACT 2002+ method, all types of midpoint categories can be linked to damage categories (DC_i), where:

- human health (DC_1) = *f(C, NC, RI, IR, OLD,RO)*;
- ecosystem quality (DC_2) = *f(AET, TET, TAN, LO, AA, AE)*;
- climate change (DC_3) = *f(GWP)*;
- resources (DC_4) = *f(NRE, ME)*.

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

Scale	Bench	Pilot	Ind1	Ind2	Ind3
Vessel volume, L	0.5	5.2	50	100	200
CO_2 flow rate, kg/h	2.2	22	212	440	880
Sample diameter, m	0.02	0.06	0.16	0.22	0.28
Samples per batch	4	8	18	22	28

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

Phase	Input/Output	Unit	Bench	Pilot	Ind1	Ind2	Ind3
Gelatinization	Starch	kg	6.54E-01	6.54E-01	6.54E-01	6.54E-01	6.54E-01
	Water	kg	3.71E+00	3.71E+00	3.71E+00	3.71E+00	3.71E+00
	Electricity	MJ	9.90E+03	5.50E+02	6.87E+01	4.46E+01	2.89E+01
Retrogradation	Cooked starch	kg	4.36E+00	4.36E+00	4.36E+00	4.36E+00	4.36E+00
	Electricity for cooling	MJ	1.18E+03	6.58E+01	4.11E+00	1.78E+00	8.63E-01
Alcogel 40 %	Hydrogel	kg	4.36E+00	4.36E+00	4.36E+00	4.36E+00	4.36E+00
	Ethanol	kg	3.45E+00	3.06E+00	2.87E+00	2.85E+00	2.81E+00
	Water	kg	6.55E+00	5.82E+00	5.45E+00	5.41E+00	5.34E+00
	Output						
	Ethanol	kg	2.69E+00	2.31E+00	2.12E+00	2.10E+00	2.06E+00
	Water	kg	8.82E+00	8.10E+00	7.73E+00	7.69E+00	7.62E+00
Alcogel 100 %	Alcogel 40 %	kg	2.84E+00	2.84E+00	2.84E+00	2.84E+00	2.84E+00
	Ethanol	kg	8.62E+00	7.66E+00	7.18E+00	7.12E+00	7.04E+00
	Output						
	Ethanol	kg	7.33E+00	6.38E+00	5.90E+00	5.84E+00	5.75E+00
	Water	kg	2.18E+00	2.18E+00	2.18E+00	2.18E+00	2.18E+00
Drying	Alcogel 100 %	kg	1.94E+00	1.94E+00	1.94E+00	1.94E+00	1.94E+00
	Carbon dioxide	kg	1.73E+03	9.63E+02	5.79E-02	5.01E-02	4.86E-02
	Electricity	MJ	2.47E+03	6.74E+02	6.06E+01	4.96E+01	6.98E+01
	Electricity for cooling	MJ	4.54E+02	1.45E+02	2.46E+01	1.96E+01	1.34E+01
	Output						
	Aerogel	kg	1.00E+00	1.00E+00	1.00E+00	1.00E+00	1.00E+00
	Carbon dioxide	kg	1.73E+03	9.63E+02	5.79E-02	5.01E-02	4.86E-02
	Ethanol	kg	9.36E-01	9.36E-01	9.36E-01	9.36E-01	9.36E-01

3. Results and discussion

The aim of this study is the environmental analysis of the production of starch aerogel on different scales. Table 4 shows the IMPACT 2002+ results at midpoint level for aerogel production on real scales (bench and pilot) and on simulated scales. It is evident that the impacts obtained in the simulations on industrial scales are definitely lower with respect to the real scales. This is due to the assumptions made to perform the simulation. Indeed, in the bench and in the pilot plant, carbon dioxide after drying is released at atmosphere, because of the low flow rates, whereas in the industrial plants, it is condensed and recycled. Observing the values shown in Table 4, it is evident that the scale-up of the process up to industrial scale is recommended, not only from the economical point of view, but also from the environmental point of view.

The results obtained in terms of midpoint categories were, then, grouped considering the four damage categories and are shown in Figure 2. Considering that, also at endpoint level, the impacts are expressed in four different units, they were normalized, according to the reference document for IMPACT 2002+ method (Humbert at al., 2012). Due to normalization, the global damage (GD) can be expressed as:

$$GD = \sum_{i=1}^{4} DC_i \quad (1)$$

Therefore, we report in Figure 3 the trend of GD with respect to the scale of the plant. It is evident that, once reached the industrial scale, the impact is practically independent from the dimensions of the vessel, reaching a plateau value.

Table 4: IMPACT 2002+ impacts at midpoint level.

Impact	Unit	Bench	Pilot	Ind1	Ind2	Ind3
Carcinogens	kgC_2H_3Cleq	1.01E+02	2.96E+01	4.94E+00	4.29E+00	4.24E+00
Non-carcinogens	kgC_2H_3Cleq	3.49E+01	1.18E+01	1.42E+00	1.20E+00	1.19E+00
Respiratory inorganics	kgPM2.5eq	2.83E+00	8.53E-01	1.19E-01	1.01E-01	9.93E-02
Ionizing radiation	BqC-14eq	5.66E+04	1.18E+04	2.37E+03	1.97E+03	1.94E+03
Ozone layer depletion	kgCFC-11eq	4.15E-04	7.15E-05	1.78E-05	1.48E-05	1.45E-05
Respiratory organics	kgC_2H_4eq	5.05E+00	3.97E+00	3.56E+00	3.52E+00	3.48E+00
Aquatic ecotoxicity	kgTEGwater	1.94E+05	4.91E+04	8.20E+03	6.90E+03	6.79E+03
Terrestrial ecotoxicity	kgTEGsoil	5.09E+04	1.30E+04	2.15E+03	1.81E+03	1.78E+03
Terrestrial acid/nutri	kgSO_2eq	4.84E+01	1.29E+01	2.10E+00	1.77E+00	1.75E+00
Land occupation	m^2org.arable	4.00E+01	1.03E+01	1.69E+00	1.42E+00	1.40E+00
Aquatic acidification	kgSO_2eq	1.68E+01	4.65E+00	7.17E-01	6.06E-01	5.98E-01
Aquatic eutrophication	kgPO_4P-lim	5.17E-01	1.75E-01	3.12E-02	2.80E-02	2.77E-02
Global warming	kgCO_2eq	3.50E+03	8.84E+02	1.52E+02	1.29E+02	1.27E+02
Non-renewable energy	MJprimary	5.42E+04	1.25E+04	2.66E+03	2.29E+03	2.26E+03
Mineral extraction	MJsurplus	2.07E+02	7.87E+01	8.25E+00	7.04E+00	6.98E+00

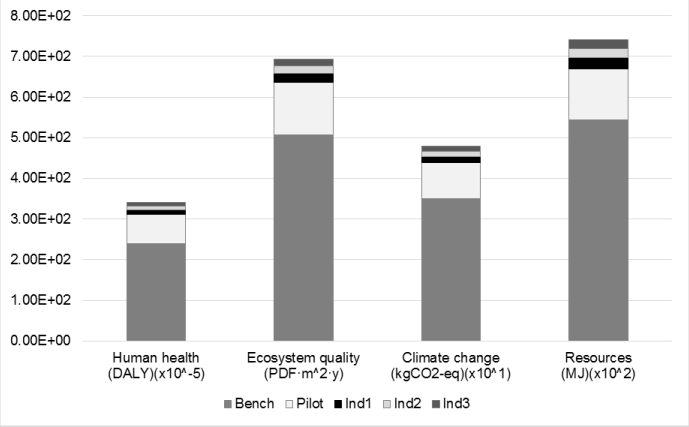

Figure 2: Impacts related to aerogel production at endpoint level.

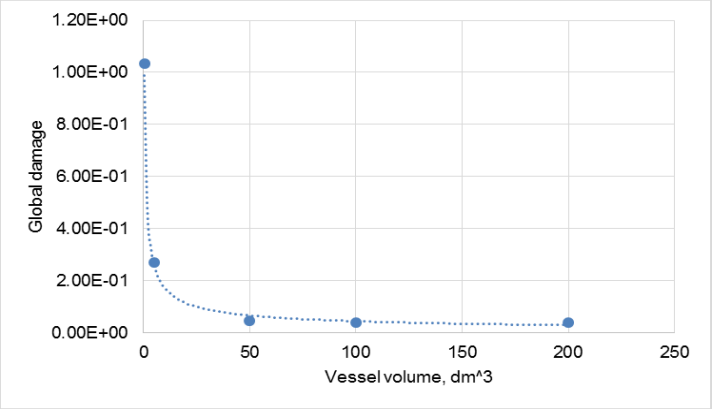

Figure 3: Global damage at different scales for functional unit.

4. Conclusions

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 emissions were strongly lowered increasing the scale of the plant. 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. A simulation on industrial scale (with vessel volumes of the dryers typical of pharmaceutical industries) was performed, demonstrating that, once reached the industrial scale, the total impact for functional unit is indipendent on the volume of the vessel. The results obtained in this gate-to-gate analysis are valid also for other aerogels obtainable using the same production process. Further studies regarding the LCA analysis of pharmaceutical principles adsorbed on starch aerogel or on similar supports will be performed.

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