Life cycle assessment of supercritical impregnation: starch aerogel + α-tocopherol tablets

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The environmental impacts of starch aerogel (SA) loaded with vitamin E (α-tocopherol, TOC) using supercritical carbon dioxide impregnation were evaluated, following a Life Cycle Assessment (LCA) approach. All the emissions to air, water and soil were reported to a 120 mg SA tablet containing the daily therapeutic dose of TOC (15 mg). The life cycle inventory was built using primary data and the LCA analysis was conducted using SimaPro 8.5.2 software. The performed analysis showed that the stages most affecting the environmental categories under study are the agricultural stages, the supercritical drying for the attainment of the aerogel and the supercritical impregnation. Solutions aimed at minimizing the impacts of these steps were proposed.

Keywords: starch aerogel; supercritical impregnation; vitamin E; minimized emissions; process optimization; sustainability.

1. Introduction

Natural antioxidants such as flavonoids, phenolic acids, carotenoids, and tocopherols are widely used as free radicals scavengers, pro-oxidative metals chelators, singlet oxygen and photosensitizers quenchers and lipoxygenase inactivators [1, 2]. Vitamin E is the term for a group of tocopherols and tocotrienols, of which α-tocopherol is the most abundant in nature and has the highest biological activity [3]. Considering that vitamins are sensitive molecules, they have to be preserved from pro-oxidant elements which could affect their chemical integrity and decrease their physiological potencies [4]. Moreover, lipophilic vitamins, such as α-tocopherol, are poorly water-soluble and have a slow dissolution rate [5].

In order to both preserve fat soluble vitamins from light, moisture, and oxygen and improve their dissolution rate, different approaches can be used [6]. Commonly, encapsulation methods based on size-reduction techniques are proposed, with the aim of obtaining microspheres or microcapsules [7, 8]. An alternative way is the charging of the active compound on a biocompatible substrate, which can be a film [9, 10], a membrane [11, 12] or an aerogel [13].

Due to their low density, large open pores, and large internal surface area, aerogels are promising candidates as matrices and carriers for active substances [14, 15]. They can be obtained from hydrogel precursors using either supercritical drying [16] or freeze drying [17]. Despite the outstanding properties of silica aerogels in terms of porosity and surface areas [18, 19], they are biocompatible but not biodegradable, and, therefore, they are not enzymatically decomposed in the body [19]. On the contrary, polysaccharide-based aerogels accomplish the biodegradability that silica aerogel lacks and, therefore, can be used as carriers in nutraceutical and pharmaceutical fields [20]. In the last years, starch, being one of the most abundant and low–cost polysaccharides, has been used as carrier for controlled delivery of drugs and vitamins [13, 21, 22]. The active substance can be adsorbed (impregnated) into the porous structure through supercritical carbon dioxide ($scCO_2$) impregnation [15, 19, 21]. The process is based on the dissolution of the active principle in $scCO_2$ and on the impregnation of the porous aerogel by its exposure to this supercritical solution. In a previous work, De Marco and Reverchon demonstrated that α-tocopherol can be incorporated into starch aerogel through $scCO_2$ impregnation, obtaining a loaded aerogel with a vitamin's dissolution rate 16 times faster with respect to the unprocessed α-tocopherol [21].

Even though supercritical fluids' based processes are considered as "eco-friendly", it is important to study the environmental emissions due to a specific production. The environmental impact of a process or a product can be determined, in a quantitative way, using the life cycle assessment (LCA) analysis. Indeed, in the last years, many papers based on LCA analyses were published in different research fields, such as energy [23], beverages [24, 25], coffee [26, 27], food [28-31], pharmaceutical delivery systems [32, 33] and wastewater treatments [34]. In particular, literature related to pharmaceuticals' LCA studies has been limited to few papers. For example, Wernet et al. carried out a LCA of the production of a pharmaceutical principle, without indicating its name for confidential reasons [33], whereas Jiménez-González et al. identified and analyzed the environmental impacts of a typical active pharmaceutical ingredient synthesis, focusing the attention in the optimization of the solvent use with the aim of reducing the impacts [35].

Concerning papers on LCA of biodegradable aerogels, an environmental study on starch aerogel production on different scale plants was performed by De Marco et al. [32], but a complete study including also the impregnation of an active principle into the porous structure was not carried out until now.

Therefore, the aim of this study is the LCA analysis of the production (using $scCO_2$ impregnation) of a 120 mg starch aerogel (SA) tablet containing the daily therapeutic dose of α-tocopherol (TOC). In the LCA analysis, the considered steps are corn cultivation, attainment of starch from corn, aerogel production from starch, and supercritical impregnation of α-tocopherol in the aerogel. Data regarding the industrial stages of the process were collected from an Italian processor.

2. Process description

In Table 1, the details of the process under analysis and the main activities are reported.

Table 1: Process details and assumptions.

Process	Characteristics and details
Energy supply to facility	Italian energy mix medium voltage
Corn cultivation	Energy, diesel and water supply Fertilizers (Nitrogen, phosphorous and potassium) supply
Corn conversion to starch	Energy, water, and fuel supply
Starch supply to facility	Transport by truck, 28 t from Mantua (distance = 700 km)

Hydrogel formation	
Gelatinization 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=48 h; ethanol and water supply; energy supply
Aerogel formation	
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=4 h; carbon dioxide supply; energy supply
Depressurization	T=25 °C; P=1 bar; t=0.33 h
Supercritical impregnation	
Stabilization	t=0.33 h; carbon dioxide supply; energy supply
Impregnation	T=60 °C; P=150 bar; t=24 h; carbon dioxide supply; energy supply
Depressurization	T=25 °C; P=1 bar; t=1 h

The used corn is cultivated in Italy in the province of Mantua and a local processor converts it into starch. After the conversion, corn starch is transported to a South Italy processor by truck. Then, it has to be prepared in form of aerogel and, subsequently, TOC can be impregnated into the prepared support.

2.1 Aerogel preparation

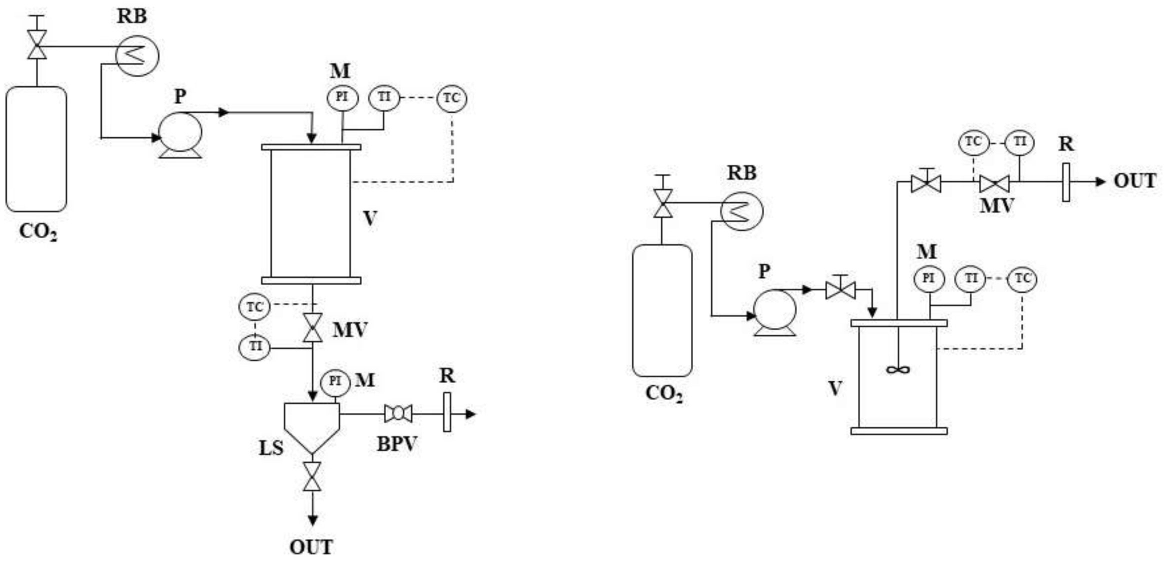
The aerogel preparation was previously optimized [36] and consisted in three steps: (a) hydrogel, (b) alcogel and (c) aerogel formation:

(a) The hydrogel can be obtained through gelatinization and retrogradation of starch granules. The gelatinization is obtained solubilizing starch in distilled water at a concentration of 15 % w/w, stirring the solution for 24 h at 75 °C, and pouring the structure called "cooked starch" into cylindrical moulds. The retrogradation is the rearrangement of the structure, obtained by putting the samples in a refrigerator at 4 °C for three days.

(b) The alcogel is obtained replacing the water filling the pores of the hydrogel by batch equilibration using two ethanol baths at increasing concentration (40 % and 100 % (v/v)) at room temperature. Each ethanol bath contains two volumes of liquid for each volume of gel and the equilibration time for each bath is 24 h [32].

(c) The aerogel is obtained through a supercritical drying at 20 MPa, 45 °C for 4 h [21, 32, 36]. In an experimental test performed at industrial scale, the alcogel samples are placed in a 100 L volume vessel, heated through a heating jacket using vapour at 150 °C and 0.1 MPa; the vapour is produced in a burner using methane as fuel. The vessel, through a high-pressure pump, is filled from the top with supercritical carbon dioxide. Carbon dioxide is cooled using cooling water at 10 °C, before pumping, to avoid cavitation. The $scCO_2$

flow rate is fixed at 440 kg/h, corresponding to a residence time inside the vessel of about 4 min. A rotameter measures CO_2 flow rate and the carbon dioxide is recycled, after condensation, in a horizontal exchanger with a square pitch and 4 tube passes.



(a) *(b)*

Figure 1: Sketches of the plants for (a) drying of aerogel and (b) impregnation experiments. CO_2: carbon dioxide supply; RB: refrigerating bath; P: pump; V: vessel; TC: temperature controller; TI: temperature indicator; M: manometer; MV: micrometering valve; LS: liquid separator; BPV: back-pressure valve; R: rotameter.

2.2 Supercritical impregnation

Impregnation experiments were performed using a static method [19, 37]. Briefly, a known amount of aerogel (about 100 g) was wrapped in filter paper placed on the bottom of the vessel (V=20 L), to avoid its contact with the vitamin (TOC) in the liquid state. In order to allow contact with $scCO_2$, a weighed amount of TOC was placed in a container opened on the top mounted axially on the impeller. The autoclave was, then, closed, heated to the fixed temperature and slowly filled with CO_2. After the working pressure (15 MPa) was reached, the system was stored for 24 h, which assured the dissolution of the vitamin in $scCO_2$ and the attainment of the adsorption equilibrium. Indeed, the impregnation time depends by the vessel volume [38] and by the vitamin's solubility in the supercritical carbon dioxide in correspondence of the chosen pressure and temperature. The amount of carbon dioxide in the vessel was determined from the density value (given at the test temperature and pressure), and, at 15 MPa and 60 °C, it was equal to 12 kg. Then, CO_2 was vented out at constant flow rate (about 1 MPa/min) and recycled, after condensation. When temperature and pressure in the vessel were equal to the ambient, the aerogel was removed from the autoclave and weighted.

The weight increase of the aerogel indicated the amount of loaded vitamin.

3. LCA methodology

Data regarding the life cycle of the entire process (drying + impregnation) can be correlated through the LCA analysis, in order to identify the phases of the process that are critical from an environmental point of view. The main steps of the analysis are described in the following part of this section.

3.1 Goal definition, functional unit and system boundaries

The goal definition is one of the most important phases of the LCA methodology, because the whole study will be influenced by the choices made in this step. In particular, the goal of this study is the evaluation of the environmental impacts related to the attainment of a SA tablet loaded with TOC. Both the aerogel production and the TOC impregnation are obtained through $scCO_2$ based techniques.

Another important step of an LCA analysis is the definition of the functional unit (FU), which is the reference to which inputs and outputs of the process have to be related. In this work, the FU was defined as a 120 mg SA tablet containing the daily therapeutic dose of TOC (15 mg).

Through mass and energy balances of each operation constituting the process, a cradle-to-factory gate analysis was performed; therefore, the system boundaries (reported in Figure 2) are set from corn cultivation to impregnated aerogel attainment. The use phase and disposal phase of the product were not considered in this study.

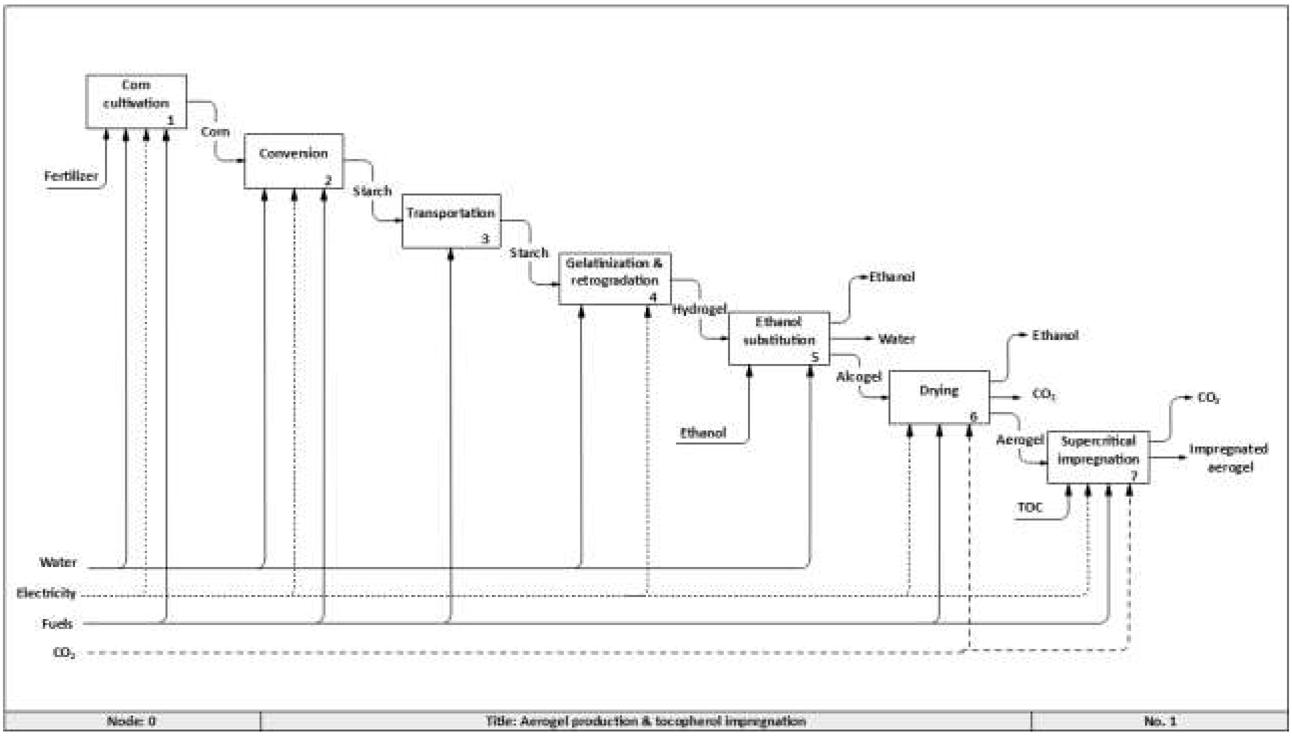


Figure 2: IDEF diagram of aerogel production and tocopherol impregnation.

3.2 Data collection and life cycle inventory

The life cycle inventory (LCI) is one of the most time-consuming steps and the quality and repeatability of an LCA study is strongly dependent on the quality of data handled in this step. LCI consists in the search, collection, and interpretation of data regarding each step of the process. All inputs and outputs regarding resources, water, electricity and fuels have to be collected and quantified with respect to the chosen functional unit. Inventory data regarding the TOC extraction from the microalgae *Tetraselmis suecica* were recovered from literature [39]. A Northern Italy processor supplied data regarding the corn cultivation and its conversion into starch; these data were collected on-site and corresponded to the amounts of chemicals, water and electricity used to obtain starch. Data regarding the starch aerogel production and its impregnation with TOC were collected directly from the production site, thanks to a Southern Italy processor, which uses supercritical carbon dioxide based processes in the attainment of aerogel and in the impregnation process. The electricity consumptions in each step of the process were evaluated considering the different constituents of the plants. Background inventory data, consisting in the production of chemicals, fertilizers, and electricity (Italian energy mix) were taken from the Ecoinvent 3.4 database. All the data were organized in tables constituting the inventory through mass and energy balances made on each step of the production process. The resulting inventory for the inputs and outputs of the different main steps is shown in Table 2.

Table 2: Life cycle inventory of the main inputs and outputs for starch aerogel production, and tocopherol impregnation on starch aerogel with respect to 120 mg tablet.

Production Phase	Input/Output	Unit	
Agricultural	Water	m^3	2.25E-03
	Diesel	kJ	2.86E+01
	Fertilizers	g	5.61E-01
	Electricity	kJ	8.97E+00
Transportation	Starch	g	6.87E-02
	Transport by truck	tkm	3.25E-04
Gelatinization step	Starch	g	6.87E-02
	Water	g	3.89E-01
	Electricity	kJ	2.08E+00
Retrogradation step	Hydrogel	g	4.58E-01
	Electricity for cooling	kJ	2.49E-01
Alcogel 40 %	Hydrogel	g	4.58E-01
	Ethanol	g	3.62E-01
	Water	g	6.87E-01
	Output		
	Ethanol	g	2.83E-01
	Water	g	9.26E-01
Alcogel 100 %	Alcogel 40 %	g	2.98E-01
	Ethanol	g	9.05E-01
	Output		
	Ethanol	g	7.70E-01
	Water	g	2.29E-01
Drying	Alcogel 100 %	g	2.03E-01
	Carbon dioxide	g	7.28E+00
	Methane	g	3.73E-02
	Electricity	kJ	1.25E+02
	Electricity for cooling	kJ	2.74E+00
	Output		
	Carbon dioxide	g	7.28E+00
	Ethanol	g	9.83E-02
Impregnation	Aerogel	g	1.05E-01
	Carbon dioxide	g	5.05E-02
	α-tocopherol	g	1.50E-02
	Methane	g	3.60E-01
	Electricity	kJ	1.05E+00
	Electricity for cooling	kJ	4.21E-02
	Output		
	Impregnated aerogel	g	1.20E-01
	Carbon dioxide	g	5.05E-02

3.3 Impact assessment

The elaboration of the inventory data was performed through the LCA software SimaPro 8.5.2 (PRé Consultants, 2018) in agreement with the reference standard for LCA (i.e. ISO 14040-14044). ReCiPe method [40] was used to aggregate the inventory results first in terms of 18 midpoint categories and, then, in terms of damages to human health, ecosystem diversity and resource availability (endpoint). The list of the impact categories at midpoint and endpoint level assessed in the present study is shown in the first column of Table

3. In the second and third column of Table 3, the impact categories' acronyms and the units in which they are measured are reported. ReCiPe method proposed three cultural perspectives, representing choices on time or on expectations linked to the development of future technologies that should avoid future damages: the "individualist" is a short term optimistic perspective, the "hierarchist" is a consensus model, and the "egalitarian" is a long term perspective based on precautionary principle thinking [40]. The chosen time perspective in this study is the hierarchist (H), which is based on the most common policy principles concerning time-frame and is the most balanced one.

Table 3: Environmental impact categories with their respective acronyms and units and impact assessment at midpoint level with respect to 120 mg tablet.

Impact category	Acronym	Unit	Impact assessment
Midpoint level			
Climate change	CC	kg CO_2 eq	2.53E-02
Ozone depletion	OD	kg CFC-11 eq[1]	2.37E-09
Terrestrial acidification	TA	kg SO_2 eq	1.25E-04
Freshwater eutrophication	FE	kg P eq	8.99E-06
Marine eutrophication	ME	kg N eq	1.42E-05
Human toxicity	HT	kg 1,4DCB eq[1]	8.14E-03
Photochemical oxidant formation	POF	kg NMVOC[1]	9.01E-04
Particulate matter formation	PMF	kg PM_{10} eq	4.01E-05
Terrestrial ecotoxicity	TET	kg 1,4DCB eq[1]	1.10E-05
Freshwater ecotoxicity	FET	kg 1,4DCB eq[1]	8.37E-04
Marine ecotoxicity	MET	kg 1,4DCB eq[1]	7.39E-04
Ionising radiation	IR	kBq U235 eq[1]	3.33E-03
Agricultural land occupation	ALO	m^2 x yr	3.15E-03
Urban land occupation	ULO	m^2 x yr	2.65E-04
Natural land transformation	NLT	m^2	3.07E-06
Water depletion	WD	m^3	5.12E-04
Mineral resource depletion	MRD	kg Fe eq	1.10E-03
Fossil fuel depletion	FD	kg oil eq	7.24E-03
Endpoint level			
Human health	HH	DALY[1]	
Ecosystem diversity	ED	species.yr	
Resource availability	RA	$	

[1]CFC-11: Chlorofluorocarbon; 1,4DCB: 1,4 dichlorobenzene; NMVOC: Non Methane Volatile Organic Carbon compound; U235: Uranium 235; DALY: disability-adjusted life years; species.yr: loss of species during a year; $: increased cost.

4. Results and discussion

4.1 Environmental analysis of aerogel + TOC formation

The environmental analysis of the production of starch aerogel loaded with TOC was performed in terms of ReCiPe midpoint categories. The analysis was performed considering the production of a 120 mg tablet containing the 15 mg daily therapeutic dose of vitamin E; the results of the impact assessment due to the cradle-to-factory gate production are reported in the last column of Table 3.

In order to identify the processing steps that generate the higher impact, an in-depth analysis was performed. The impact assessments at midpoint level related to each stage of the process are reported in Table 4.

Table 4: Impact assessment at midpoint level with respect to 120 mg tablet.

Impact category	corn cultivation	conversion to starch	transportation	hydrogel	alcogel	aerogel	TOC impregnation
CC	4.17E-04	4.68E-04	7.24E-05	2.65E-04	1.59E-03	2.10E-02	1.54E-03
OD	2.17E-11	4.64E-11	9.95E-11	3.19E-11	4.56E-11	2.02E-09	1.05E-10
TA	4.07E-06	4.37E-06	5.27E-07	1.28E-06	5.24E-06	9.08E-05	1.83E-05
FE	1.68E-07	1.83E-07	2.00E-10	8.81E-08	6.71E-07	7.00E-06	8.74E-07
ME	2.20E-06	5.60E-06	3.06E-08	5.41E-08	1.70E-07	4.78E-06	1.37E-06
HT	1.02E-04	1.98E-04	9.31E-06	8.13E-05	3.39E-04	6.91E-03	4.98E-04
POF	1.38E-06	1.52E-06	9.75E-07	5.93E-07	7.16E-04	1.11E-04	3.43E-06
PMF	1.13E-06	1.17E-06	2.19E-07	3.83E-07	1.98E-06	3.13E-05	3.91E-06
TET	3.32E-06	2.23E-06	9.29E-09	3.81E-08	9.45E-08	3.86E-06	1.45E-06
FET	5.67E-06	6.38E-06	3.82E-08	1.28E-05	7.95E-06	7.68E-04	3.62E-05
MET	3.62E-06	4.92E-06	9.32E-08	1.12E-05	7.88E-06	6.79E-04	3.21E-05
IR	1.70E-05	3.97E-05	1.13E-05	4.79E-05	2.79E-05	2.97E-03	2.17E-04
ALO	4.71E-04	7.90E-04	0.00E+00	2.54E-05	4.93E-05	1.61E-03	2.01E-04
ULO	2.48E-05	1.86E-05	0.00E+00	2.86E-06	8.74E-06	1.99E-04	1.13E-05
NLT	7.23E-08	7.99E-08	0.00E+00	3.38E-08	9.28E-08	2.51E-06	2.81E-07
WD	1.11E-04	1.27E-05	5.03E-07	5.21E-06	1.42E-05	3.21E-04	4.62E-05
MRD	1.92E-05	4.42E-05	3.10E-06	9.13E-06	6.80E-05	8.95E-04	6.13E-05
FD	8.07E-05	1.03E-04	2.49E-05	7.45E-05	1.27E-03	5.37E-03	3.12E-04

The relative contributions of the different stages of the complete process are reported in Figure 3, where the corn cultivation and its conversion into starch were grouped in the “starch production” stage.

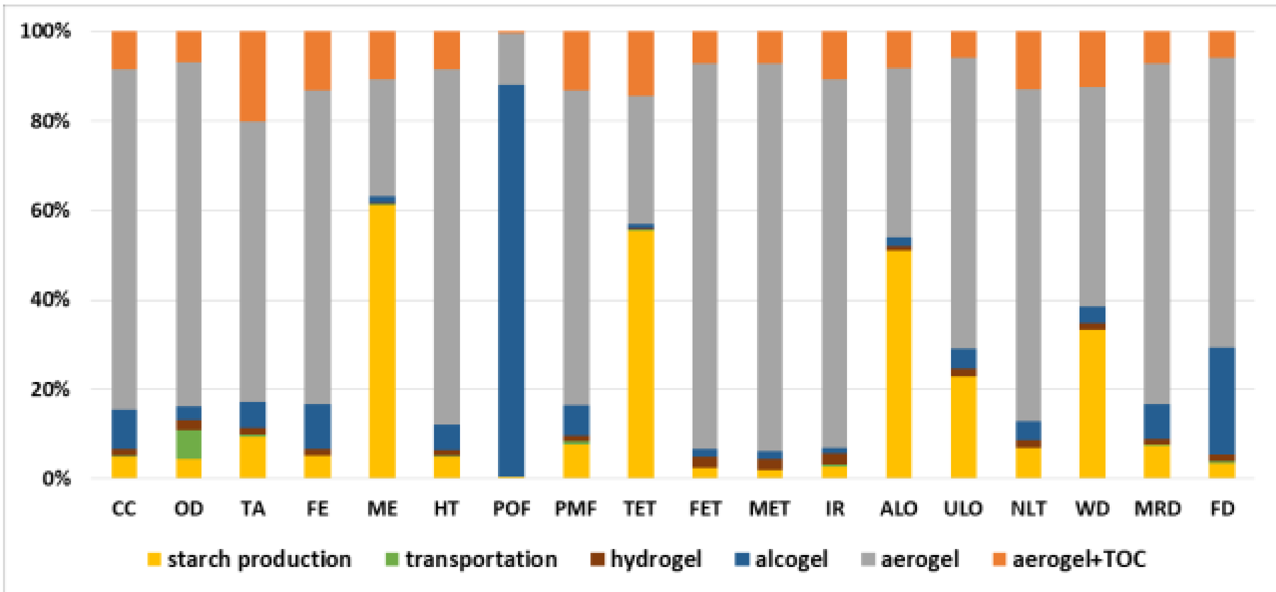


Figure 3. Relative contributions of the different stages with respect to the overall impact.

The contribution of each production stage on the midpoint impact categories may be immediately visualized in the heat map reported in Table 5, where the cell colors (and the fonts) are assigned based on the value of the impact. The color scale is green to yellow to red, with low contribution to the impact getting the green color (italic) and high contribution to the impact getting the red color (bold).

Table 5. Heat map of the process stages with respect to the overall impact.

impact category	starch production	transportation	hydrogel	alcogel	aerogel	aerogel+TOC	entire process
Climate change	3.5%	*0.3%*	*1.0%*	6.3%	**55.1%**	6.1%	100%
Ozone depletion	2.9%	4.2%	*1.3%*	*1.9%*	**49.6%**	4.4%	100%
Terrestrial acidification	6.8%	*0.4%*	*1.0%*	4.2%	**45.5%**	14.7%	100%
Freshwater eutrophication	3.9%	*0.0%*	*1.0%*	7.5%	**51.9%**	9.7%	100%
Marine eutrophication	**54.9%**	*0.2%*	*0.4%*	*1.2%*	23.5%	9.6%	100%
Human toxicity	3.7%	*0.1%*	*1.0%*	4.2%	**58.4%**	6.1%	100%
Photochemical oxidant formation	*0.3%*	*0.1%*	*0.1%*	**85.8%**	11.4%	*0.4%*	100%
Particulate matter formation	5.7%	*0.5%*	*1.0%*	4.9%	**52.7%**	9.8%	100%
Terrestrial ecotoxicity	**50.5%**	*0.1%*	*0.3%*	*0.9%*	25.8%	13.2%	100%
Freshwater ecotoxicity	*1.4%*	*0.0%*	*1.5%*	*0.9%*	**51.3%**	4.3%	100%
Marine ecotoxicity	*1.2%*	*0.0%*	*1.5%*	*1.1%*	**51.7%**	4.4%	100%
Ionising radiation	*1.7%*	*0.3%*	*1.4%*	*0.8%*	**51.0%**	6.5%	100%
Agricultural land occupation	**40.0%**	*0.0%*	*0.8%*	*1.6%*	29.8%	6.4%	100%
Urban land occupation	16.4%	*0.0%*	*1.1%*	3.3%	**46.3%**	4.3%	100%
Natural land transformation	5.0%	*0.0%*	*1.1%*	3.0%	**52.5%**	9.2%	100%
Water depletion	24.2%	*0.1%*	*1.0%*	2.8%	**35.8%**	9.0%	100%
Mineral resource depletion	5.8%	*0.3%*	*0.8%*	6.2%	**59.3%**	5.6%	100%
Fossil fuel depletion	2.5%	*0.3%*	*1.0%*	17.5%	**46.9%**	4.3%	100%

Observing Figure 3 and Table 5, it is evident that the contributions of starch transportation step and hydrogel formation step are negligible on all the ReCiPe midpoint categories. The corn cultivation and its transformation into starch (grouped in the "starch production" column) are high in terms of marine eutrophication (54.9 %), terrestrial ecotoxicity (50.5 %) and agricultural land occupation (40.0 %). The alcogel production has a high contribution (85.8 %) on photochemical oxidant formation, because of the high quantity of ethanol used in solvent exchanges to transform the hydrogel in alcogel. The supercritical drying (aerogel formation) is the major contributor to all the midpoint categories, with an exception for ME, POF, TET and ALO. The supercritical impregnation of TOC onto the aerogel has an appreciable contribution (at least 5 %) in terms of all the categories with an exception for OD, POF, FET, MET, ULO and FD. In both the supercritical based processes, the emissions are due to the high consumption of electrical energy, mainly related to the condensation and recycling of carbon dioxide.

4.2 Scenario analysis and improved solution

Considering that the emissions on some impact categories may be reduced if proper industrial choices are made, a scenario analysis is proposed. The possible interventions on the early stages of the process (starch production) were not taken into account, considering that those stages are not responsibility of the TOC charged aerogel processor. Drying pressure, temperature and time modifications were not considered, because these variables were chosen in order to optimize the attainment of the porous structure of the aerogel [36]. Moreover, the effect of the reduction of the impregnation time was not investigated, because in correspondence of the chosen time, the maximum amount of α-tocopherol was impregnated onto the starch aerogel [21].

The proposed scenario analysis considers: (a) the possibility of recycling (in the alcogel formation stage) part of the ethanol; (b) the reduction of the consumption due to the carbon dioxide condensation.

Therefore, different scenarios were proposed, considering:

- the recovery of part of the ethanol (33 or 66 %) from the water/ethanol mixture using a rotary evaporator, with the consequent reuse of the organic solvent in the alcogel formation step;
- the use of cooling water at a lower temperature (8.5 or 7 °C), considering the withdrawal of the water from the well at different depths.

The results of the scenario analysis are shown in the radar charts in Figure 4.

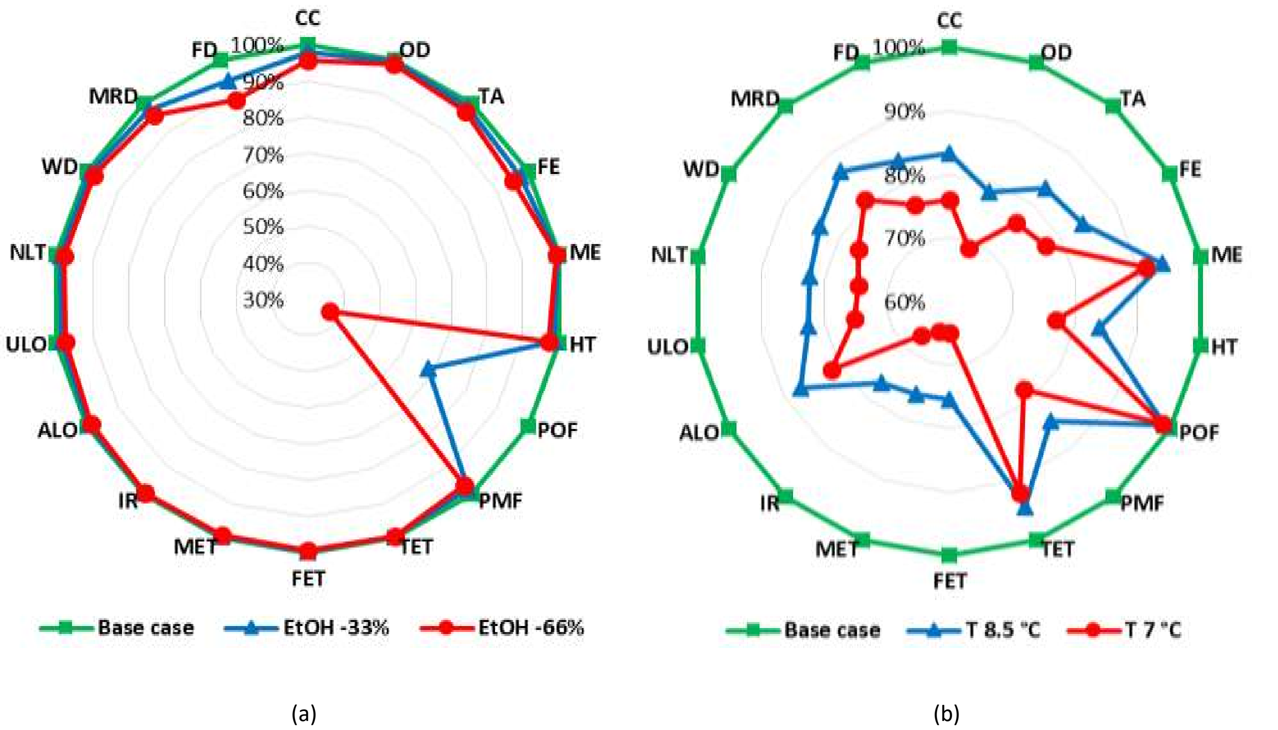


Figure 4: Scenario analysis at midpoint level: (a) different amount of the recycled ethanol; (b) different temperatures of the cooling water.

It is evident from Figure 4a that the recycling of ethanol drastically reduced the emissions in terms of photochemical oxidant formation (POF). Indeed, the environmental impact due to this category is strictly related to the presence of volatile organic compounds (VOCs) that, in presence of nitrogen oxides (NOx), formed through a photochemical oxidation tropospheric ozone (O_3), which is a toxic air pollutant and greenhouse gas [41]. Reducing the amount of organic solvents, the VOCs and therefore the tropospheric O_3 formation is deeply reduced.

It is possible to observe from Figure 4b that the water supply at different well depths; i.e., at different temperatures, lowered the emissions in terms of all the ReCiPe midpoint categories.

On the basis of the performed analysis, an improved scenario is proposed, considering the recycling of the 66 % of ethanol and the use of cooling water at 7 °C. In Table 6, the emissions at midpoint level of this improved scenario and its comparison with the base case (use of not recycled ethanol and cooling water at 10 °C) are reported.

Table 6. Impact assessment at midpoint level of the improved scenario ant its comparison with the base case. Data are referred to the production of a 120 mg SA tabled impregnated with TOC.

Impact category	Base case (a)	Improved scenario (b)	Emissions' reduction with respect to the base case $\frac{(b-a)}{a} x100$
CC	2.53E-02	1.82E-02	-28.3%
OD	2.37E-09	1.61E-09	-32.3%
TA	1.25E-04	9.14E-05	-26.6%
FE	8.99E-06	6.51E-06	-27.6%
ME	1.42E-05	1.28E-05	-9.6%
HT	8.14E-03	6.03E-03	-25.9%
POF	9.01E-04	3.18E-04	-64.7%
PMF	4.01E-05	2.99E-05	-25.4%
TET	1.10E-05	1.01E-05	-8.6%
FET	8.37E-04	5.38E-04	-35.8%
MET	7.39E-04	4.75E-04	-35.7%
IR	3.33E-03	2.21E-03	-33.7%
ALO	3.15E-03	2.53E-03	-19.7%
ULO	2.65E-04	1.93E-04	-27.2%
NLT	3.07E-06	2.23E-06	-27.5%
WD	5.12E-04	3.82E-04	-25.4%
MRD	1.10E-03	8.44E-04	-23.3%
FD	7.24E-03	4.67E-03	-35.5%

It is evident that the use of the improved scenario allows an appreciable reduction of the impacts on all the ReCiPe midpoint categories.

Finally, the environmental impacts were grouped and normalized, according to the ReCiPe method, considering the damage at the endpoint level; i.e., in terms of damage to human health (HH), to ecosystem diversity (ED) and to resource availability (RA). The comparison between the base case and the proposed improved scenario is reported in Figure 5.

Figure 5: Environmental impact according to the normalised ReCiPe damage categories (millipoint, mPt).

It is possible to observe that the improved solution generated a reduction of the environmental impact equal to 27.5 % in terms of human health (HH), 25.8 % in terms of ecosystem diversity (ED) and 34.7 % in terms of resource availability (RA) with respect to the base case.

5. Conclusions and perspectives

In this study, we performed a LCA analysis regarding the production of starch aerogel loaded with α-tocopherol.

Besides, the cradle-to-factory gate LCA analysis provided quantitative information of the environmental performance of the process, showing that the major contributors to the environmental impact are agricultural stages, alcogel formation and both the supercritical carbon dioxide based processes.

The scenario analysis demonstrated that the emissions related to the alcogel formation step may be reduced recycling the ethanol and that the emissions due to the supercritical processes may be reduced varying the conditions of carbon dioxide condensation. An improved solution was proposed, obtaining a global reduction of the impact with respect to the base case equal to 30.6 %.

References

[1] E. Choe, D.B. Min, Mechanisms of antioxidants in the oxidation of foods, Compr. Rev. Food Sci. Food Saf., 8 (2009) 345-358.

[2] P. Trucillo, R. Campardelli, E. Reverchon, Production of liposomes loaded with antioxidants using a supercritical CO_2 assisted process, Powder Technol., 323 (2018) 155-162.

[3] R. Brigelius-Flohe, M.G. Traber, Vitamin E: function and metabolism, FASEB J., 13 (1999) 1145-1155.

[4] M. Gonnet, L. Lethuaut, F. Boury, New trends in encapsulation of liposoluble vitamins, J. Control. Release, 146 (2010) 276-290.

[5] R. Campardelli, E. Reverchon, α-Tocopherol nanosuspensions produced using a supercritical assisted process, J. Food Eng., 149 (2015) 131-136.

[6] S. Pinnamaneni, N.G. Das, S.K. Das, Formulation approaches for orally administered poorly soluble drugs, Pharmazie, 57 (2002) 291-300.

[7] E. Allémann, J.-C. Leroux, R. Gurny, Polymeric nano- and microparticles for the oral delivery of peptides and peptidomimetics, Adv. Drug Del. Rev., 34 (1998) 171-189.

[8] E. Merisko-Liversidge, G.G. Liversidge, E.R. Cooper, Nanosizing: a formulation approach for poorly-water-soluble compounds, Eur. J. Pharm. Sci., 18 (2003) 113-120.

[9] S. Concilio, P. Iannelli, L. Sessa, R. Olivieri, A. Porta, F. De Santis, R. Pantani, S. Piotto, Biodegradable antimicrobial films based on poly (lactic acid) matrices and active azo compounds, J. Appl. Pol. Sci., 132 (2015) 42357-42364.

[10] P. Dutta, S. Tripathi, G. Mehrotra, J. Dutta, Perspectives for chitosan based antimicrobial films in food applications, Food Chem., 114 (2009) 1173-1182.

[11] L. Baldino, S. Cardea, E. Reverchon, Production of antimicrobial membranes loaded with potassium sorbate using a supercritical phase separation process, Innov. Food Sci. Emerg. Technol., 34 (2016) 77-85.

[12] J.-H. Jiang, L.-P. Zhu, X.-L. Li, Y.-Y. Xu, B.-K. Zhu, Surface modification of PE porous membranes based on the strong adhesion of polydopamine and covalent immobilization of heparin, J. Membr. Sci., 364 (2010) 194-202.

[13] M. Pantić, Ž. Knez, Z. Novak, Supercritical impregnation as a feasible technique for entrapment of fat-soluble vitamins into alginate aerogels, J. Non-Cryst. Solids, 432 (2016) 519-526.

[14] G. Caputo, I. De Marco, E. Reverchon, Silica aerogel–metal composites produced by supercritical adsorption, J. Supercrit. Fluids, 54 (2010) 243-249.

[15] I. Smirnova, S. Suttiruengwong, W. Arlt, Feasibility study of hydrophilic and hydrophobic silica aerogels as drug delivery systems, J. Non-Cryst. Solids, 350 (2004) 54-60.

[16] S. Cardea, L. Baldino, I. De Marco, P. Pisanti, E. Reverchon, Supercritical gel drying of polymeric hydrogels for tissue engineering applications, Chem. Eng. Trans., 32 (2013) 1123-1128.

[17] H. Jin, Y. Nishiyama, M. Wada, S. Kuga, Nanofibrillar cellulose aerogels, Colloids Surf. A Physicochem. Eng. Asp., 240 (2004) 63-67.

[18] S.K. Rajanna, D. Kumar, M. Vinjamur, M. Mukhopadhyay, Silica Aerogel Microparticles from Rice Husk Ash for Drug Delivery, Ind. End. Chem. Res., 54 (2015) 949-956.

[19] I. Smirnova, J. Mamic, W. Arlt, Adsorption of drugs on silica aerogels, Langmuir, 19 (2003) 8521-8525.

[20] C. García-González, M. Alnaief, I. Smirnova, Polysaccharide-based aerogels—Promising biodegradable carriers for drug delivery systems, Carbohyd. Polym., 86 (2011) 1425-1438.

[21] I. De Marco, E. Reverchon, Starch aerogel loaded with poorly water-soluble vitamins through supercritical CO_2 adsorption, Chem. Eng. Res. Des., 119 (2017) 221-230.

[22] Z. Ulker, C. Erkey, An emerging platform for drug delivery: Aerogel based systems, J. Control. Release, 177 (2014) 51-63.

[23] S. González-García, A.C. Dias, S. Clermidy, A. Benoist, V. Bellon Maurel, C.M. Gasol, X. Gabarrell, L. Arroja, Comparative environmental and energy profiles of potential bioenergy production chains in Southern Europe, J. Clean. Prod., 76 (2014) 42-54.

[24] I. De Marco, S. Miranda, S. Riemma, R. Iannone, Life Cycle Assessment of Ale and Lager Beers Production, Chem. Eng. Trans., 49 (2016) 337-342.

[25] C. Gazulla, M. Raugei, P. Fullana-I-Palmer, Taking a life cycle look at crianza wine production in Spain: Where are the bottlenecks?, Int. J. Life Cycle Assess., 15 (2010) 330-337.

[26] S. Humbert, Y. Loerincik, V. Rossi, M. Margni, O. Jolliet, Life cycle assessment of spray dried soluble coffee and comparison with alternatives (drip filter and capsule espresso), J. Clean. Prod., 17 (2009) 1351-1358.

[27] I. De Marco, S. Riemma, R. Iannone, Life cycle assessment of supercritical CO2 extraction of caffeine from coffee beans, J. Supercrit. Fluids, 133, Part 1 (2018) 393-400.

[28] J. Berlin, Environmental life cycle assessment (LCA) of Swedish semi-hard cheese, Int. Dairy J., 12 (2002) 939-953.

[29] W.K. Biswas, G. Naude, A life cycle assessment of processed meat products supplied to Barrow Island: A Western Australian case study, J. Food Eng., 180 (2016) 48-59.

[30] I. De Marco, S. Riemma, R. Iannone, Uncertainty of input parameters and sensitivity analysis in life cycle assessment: An Italian processed tomato product, J. Clean. Prod., 177 (2018) 315-325.

[31] I. De Marco, S. Miranda, S. Riemma, R. Iannone, Environmental assessment of drying methods for the production of apple powders, Int. J. Life Cycle Assess., 20 (2015) 1659-1672.

[32] I. De Marco, R. Iannone, S. Miranda, S. Riemma, An environmental study on starch aerogel for drug delivery applications: effect of plant scale-up, Int. J. Life Cycle Assess., 23 (2018) 1228-1239.

[33] G. Wernet, S. Conradt, H.P. Isenring, C. Jiménez-González, K. Hungerbühler, Life cycle assessment of fine chemical production: a case study of pharmaceutical synthesis, Int. J. Life Cycle Assess., 15 (2010) 294-303.

[34] S. Lassaux, R. Renzoni, A. Germain, Life cycle assessment of water from the pumping station to the wastewater treatment plant, Int. J. Life Cycle Assess., 12 (2007) 118-126.

[35] C. Jiménez-González, A.D. Curzons, D.J.C. Constable, V.L. Cunningham, Cradle-to-Gate Life Cycle Inventory and Assessment of Pharmaceutical Compounds, Int. J. Life Cycle Assess., 9 (2004) 114-121.

[36] I. De Marco, L. Baldino, S. Cardea, E. Reverchon, Supercritical gel drying for the production of starch aerogels for delivery systems, Chem. Eng. Trans., 43 (2015) 307-312.

[37] Y. Zhang, D. Kang, M. Aindow, C. Erkey, Preparation and characterization of ruthenium/carbon aerogel nanocomposites via a supercritical fluid route, J. Phys. Chem. B, 109 (2005) 2617-2624.

[38] P. Gurikov, I. Smirnova, Amorphization of drugs by adsorptive precipitation from supercritical solutions: A review, J. Supercrit. Fluids, 132 (2018) 105-125.

[39] P. Pérez-López, S. González-García, R.G. Ulloa, J. Sineiro, G. Feijoo, M.T. Moreira, Life cycle assessment of the production of bioactive compounds from Tetraselmis suecica at pilot scale, J. Clean. Prod., 64 (2014) 323-331.

[40] M. Goedkoop, R. Heijungs, M. Huijbregts, A. De Schryver, J. Struijs, R. van Zelm, ReCiPe 2008, A life cycle impact assessment method which comprises harmonised category indicators at the midpoint and the endpoint level, (2009).

[41] B.J. Finlayson-Pitts, J.N. Pitts, Tropospheric air pollution: ozone, airborne toxics, polycyclic aromatic hydrocarbons, and particles, Science, 276 (1997) 1045-1051.