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ORIGINAL PAPER

Life cycle assessment of hydroethanolic extracted phytotherapeutic products

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Abstract
Life cycle assessment (LCA) is a powerful method for identifying and analysing process alternatives from an environmental perspective. This methodology has been implemented in several fields; however, to date, there is no life cycle assessment of hydroethanolic-extracted phytotherapeutic products. In this study, three hydroethanolic extraction processes were evaluated, each one characterised with specific temperatures, timings, and solvent amounts. Although each process is suitable for multiple plants, this study focuses on *Passiflora incarnata*, *Calendula officinalis*, and *Vitex agnus-castus*. An environmental assessment of five phytotherapeutic products is carried out through an LCA, from cradle to gate. For each product, land use was found to be the most dominant indicator of the total environmental impact, since organic farming methods are used. In the majority of analysed products, this indicator constitutes more than 60 % of the total environmental impact. For each pack of 50 capsules, 1.33 kg of CO_{2eq} is emitted. Ethanol was found to be a significant contributor to Photochemical Ozone Formation (POF) due to its emissions into the atmosphere during the hydroethanolic extraction process, specifically during maceration. It was found that, even at a small scale, the production of phytotherapeutic products has a significant environmental footprint, mainly due to outdated and purely organic cultivation practices. Furthermore, the evaporation of the ethanol used in the extraction steps is a major contributor to the carbon footprint and POF of the products studied.

Keywords Sustainability · Life cycle assessment · SimaPro · Phytotherapy · Hydroethanolic extraction

Introduction

Medicinal treatments have been associated with human activity since ancient times, with archaeological evidence of the use of plants to cure diseases dating back 60,000 years (Matole et al. 2021). These were the first iterations of phytotherapy, where natural herbs were used to cure the most common diseases. Phytotherapy, in its purest applications, has no significant environmental impact, as only small quantities of herbs are collected and directly used, with some processes being carried out by hand, such as mashing or seed opening. This most pure type of treatment can still be found in some places on Earth, where it is used not due to environmental awareness, but rather because of a long-standing culture of using natural herbs as medicine (Atanasov et al. 2015).

Pharmaceutical products are subject to strict and rigorous regulations, leaving little to no room for improvement. Commonly, a product requires a purity close to 100 %, with strict rules on what can constitute the excipient portion (Yu and Kopcha 2017). There are significant costs, both environmental and economic, to achieve such high purities; that is why sustainability analysis is increasingly important in every sector, especially in pharmaceuticals. Several works on environmental impacts of pharmaceutical products have been carried out (Sharma et al. 2022, 2020), where it was found that in some specific cases (such as in the materials used for packaging), life cycle assessment (LCA) was able to find improved pathways to produce the same Active Pharmaceutical Ingredient (API) that are less environmentally intensive (Güneş and Şengül 2022). Another LCA study,

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using a cradle-to-gate boundary system, found that the pharmaceutical industry has a greater environmental impact than average basic chemical production, as pharmaceutical production requires high product purity and highly controlled environments (Wernet et al. 2010). The strict standards for pharmaceutical products and processes lead to high energy consumption, which in turn leads to carbon emissions. Furthermore, it was found that solvents can have a significant contribution to the environmental impacts of pharmaceutical products, since these solvents are often incinerated rather than recovered (Wilder et al. 2024). The use of LCA in the pharmaceutical industry is therefore paramount, as it can identify improved sustainable pathways to achieve the same APIs (Dias et al. 2023a, 2023).

Phytotherapeutic products are inherently less environmentally expensive than pharmaceutical products, as they use as much of the natural form of the herbs as possible. However, some phytotherapeutic products also require the use of solvents, which, if incinerated (and not recovered), can have significant environmental impacts. In the case of the phytotherapeutic products studied in this work, only hydroethanolic extractions (Félix et al. 2020); (Sullivan et al. 2010) are considered, where part of the solvent used becomes part of the final product and the remaining is emitted to the atmosphere through evaporation. In this study, the hydroethanolic extractions are performed on three medicinal plants, Passiflora incarnata, Calendula officinalis, and Vitex agnus-castus, which are widely used in phytotherapy and represent relevant case studies for the environmental assessment carried out. The hydroethanolic extractions mentioned are performed on three different plants, *Passiflora incarnata*, *Calendula officinalis*, and *Vitex agnus-castus*. These three plants were chosen because the associated extraction processes are representative of a broader group of medicinal plants that follow very similar procedures, here denoted as process types (as shown in the supplementary material), and because they correspond to some of the most relevant and frequently produced phytotherapeutic products in the collaborating laboratory.

Passiflora incarnata is a flowering plant that is native to the southern United States of America. This plant has been used to help patients with insomnia, hysteria and epilepsy and presents analgesic properties (National Institute of Diabetes and Digestive and Kidney Diseases, Passionflower, in: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury, National Institute of Diabetes and Digestive and Kidney Diseases 2020. https://www.ncbi.nlm.nih.gov/books/NBK548020 (accessed August 24, 2023, 2020); (Savage et al. 2018). The commonly used *Passiflora incarnata* extract has been studied and characterised, and is rich in flavonoids, harmala alkaloids, coumarins, maltol, phytosterols, and glycosides (National Institute of Diabetes and Digestive and Kidney Diseases, Passionflower, in: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury, National Institute of Diabetes and Digestive and Kidney Diseases 2020. https://www.ncbi.nlm.nih.gov/books/NBK548020 (accessed August 24, 2023, 2020); (Sakalem et al. 2012); (Wohlmuth et al. 2010). The flavonoids were found to be the major contributors to the anxiolytic activity of *Passiflora incarnata* extract (Sakalem et al. 2012).

Calendula officinalis, also known as marigold, is a plant native to southern Europe that is commonly used as a garden plant due to its large, yellow, and orange flowers. It is typically applied to dermatological diseases or injuries due to its healing properties, which are attributed to the presence of triterpenoids (Ataide et al. 2018). Other chemicals, such as saponins, micronutrients, flavonoids, and polysaccharides, are also present in *Calendula officinalis* extract and are responsible for its antioxidant and anti-inflammatory responses (Leach 2008); (Samai et al. 2023).

Vitex agnus-castus is a flowering shrub commonly found in Eastern Europe and the Middle East that has long been used to help regulate the feminine ovulation cycle and to act as an antioxidant. It has also been found to have a positive influence on the treatment of polycystic ovarian syndrome (Rooney and Pendry 2014) and the treatment of acne (Sağlam et al. 2007). *Vitex agnus-castus* extract is mainly composed of monoterpenes, namely 1,8-cineole and sabinene, which constitute about 50 % of its mass (Ulukanli et al. 2015); (Boujbiha et al. 2023). The plants are presented in Fig. 1.

This study presents an environmental sustainability analysis of the hydroethanolic extraction of three plants to identify potential process improvements. To achieve this, an LCA was conducted to identify the most significant contributors to the environmental impacts associated with the production of phytotherapeutic products. To the best of the authors' knowledge, no complete LCA of phytotherapeutic products obtained through hydroethanolic extraction has been published to date. This study aims to address this research gap by presenting an LCA of the hydroethanolic extraction process for three medicinal plants. The objective is to identify the main contributors to environmental impacts and potential areas for improvement. A significant challenge encountered was the lack of data on phytotherapeutic plants in existing LCA databases. The primary contribution of this study lies in its quantification of the environmental sustainability of phytotherapeutic products, thereby establishing a foundation for future research and promoting more sustainable practices in their production.

Methodology

The production process of pharmaceutical products and the LCA of the three types of processes studied are described in this section through the description of the processing at three plants. Firstly, a brief description of the processes associated

Fig. 1 Plants studied in this work. **a** *Passiflora incarnata* (Rossato et al. 2024), **b** *Vitex agnus-castus* (Rodd and Vitex agnus-castus 2011), **c** *Calendula officinalis* (Pascual 2022)

with each plant's life until the hydroethanolic extraction of the relevant components is described. After this, the LCA modelling is described, with the life cycle inventory (LCI) and the methods used for interpretation.

Type I

Type I can be best described for the application in *Passiflora incarnata*, where these are seeded in a portion of the terrain, where 0.12 hectares yield 480 g of harvested plants. After seeding, it takes 6 months to harvest, requiring no irrigation or the use of pesticides. An organic production is performed. The harvested plants, both the leaves and the rhizomes, are dried in an open yet shadowed shed for up to two weeks, depending on atmospheric conditions. The dried raw plants are then placed in sunlight for three days and stored, as graphically represented in Fig. 2.

Passiflora incarnata dried leaves and rhizomes can be used to produce phytotherapeutic capsules or concentrated extracts, which can be used in creams, for example. The first step in the preparation of these is crushing, where the leaves and rhizomes are fed into a blender and the resulting solids are screened to obtain two granulometries. The smaller granulometry is less than 1 mm. This powder-like part is stored and is later used to make phytotherapeutic capsules. The larger granulometry material is a mix of crushed leaves and rhizomes, which allows for fragments as large as 5 mm. This mix of material is the solid phase for the hydroethanolic extraction process that originates the *Passiflora incarnata* extract.

The extraction process consists of two sequential steps: maceration and percolation. The maceration step involves mixing water (800 mL, at 80 ºC), ethanol (800 mL, at room temperature), and the solids (200 g) in a container for up to 6h, with occasional stirring of the mixture. The resulting mixture is then transferred to a steel container, where 1 L of ethanol is added to ensure a total volume of 2 L at the start of

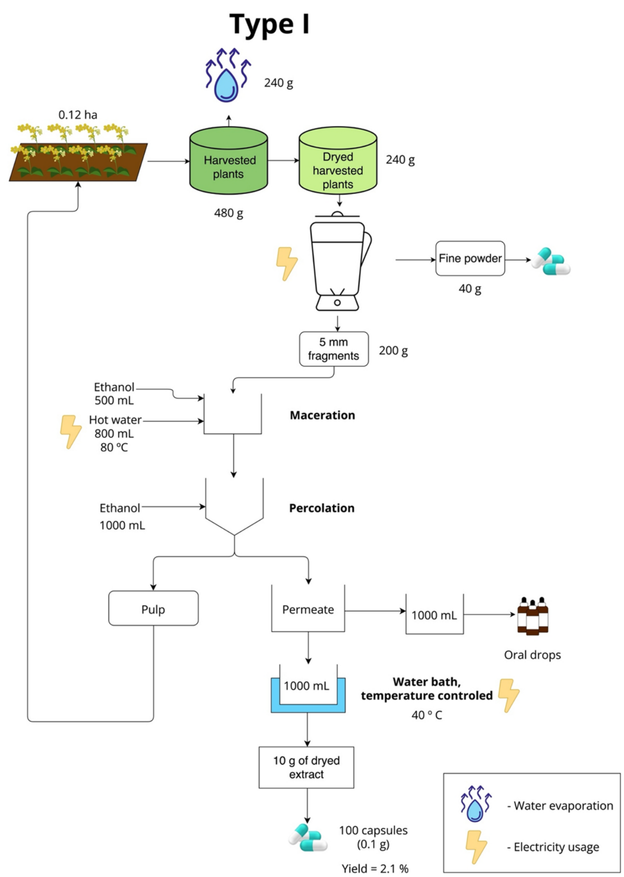

Fig. 2 Type I hydroethanolic extraction process

the percolation step. The mixture is kept in the equipment for 24h (Handa et al. 2008), after which filtration at the bottom of the container is performed, and the resulting clear mixture must have a 70 % ethanol content and a pH of 6 (Giannis 1991); (Chinniah et al. 2017). The limpid permeate obtained is the Passiflora incarnata extract, which can be directly used for oral drops or further dried in a water bath (at 80 ºC) to produce a powder for phytotherapeutic capsules, with an overall yield of 2.1 % relative to the harvested plant mass.

2.2. Type II

The type II hydroethanolic extraction is described here through its application in *Vitex agnus-castus* seeds, where 0.2 hectares yield 400 g of seeds. Similarly to Passiflora *incarnata*, Vitex agnus-castus is grown in an organic manner; however, it requires some monthly irrigation. The seeds are collected and dried but are not blended, instead, they are dipped in hot water (1000 mL, at 100 ºC) to open the seed structure, which constitutes the maceration step for the type II process, as represented in Fig. 3. In this step, 200 g of dried seeds are used, and water evaporation occurs during this stage due to the elevated temperature.

The percolation step begins with the aqueous mixture being fed to metallic equipment where 800 mL of ethanol is added to ensure a total volume of 2000 mL. The mixture is kept in this equipment for 2 days, after which the solid pulp is separated from the limpid permeate. The obtained permeate (1000 mL) can be directly used for oral drops or further dried in a glass vessel inserted into a temperature-controlled water bath at 70 ºC, yielding 10 g of dried extract, which is subsequently encapsulated to produce 100 phytotherapeutic

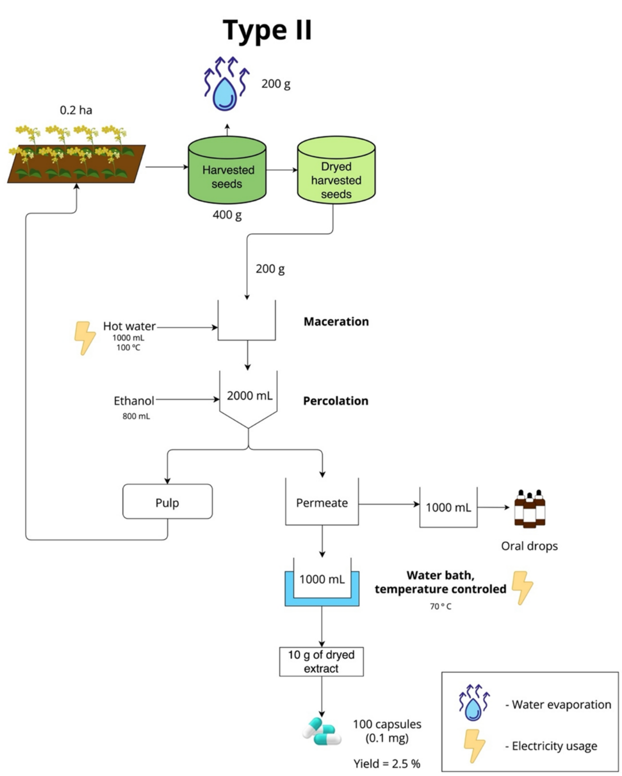

Fig. 3 Type II hydroethanolic extraction process

capsules, corresponding to an overall yield of 2.5 % relative to the harvested seeds (Giannis 1991); (fructus 2010).

Type III

Type III of hydroethanolic extraction is here described through the example of the *Calendula officinalis*, where its process starts in the *Calendula officinalis* seeds, which are grown in a breeding ground and later placed in a plot of land, where it takes up to two years for the first harvest, and half a hectare yields 60 kg of raw harvested plants. The harvested *Calendula officinalis*, whole shoot (stem and leaves), is dried in an open yet shaded shed for up to two weeks, depending on atmospheric conditions. After the shaded drying, it is placed in direct sunlight during the day for thorough drying. The dried plants are collected and stored for later use, in the case of this study, the use is hydroethanolic extraction, which starts with the preparation for the maceration step, as presented in Fig. 4. The leaves, flowers and rhizomes are fed into a blender where two granulometries of the material are obtained, a fine powder with a granulometry of less than 1 mm and a coarser granulometry of up to 5 mm. This larger granulometry material is used for the maceration step, where 200 g is mixed with equal parts of water (800 mL) and ethanol (800 mL) at room temperature. The dried blended *Calendula officinalis* flowers and rhizomes are kept in the container with the water and ethanol for three days, after which the mixture is transferred to a steel container to carry out the percolation step. The resulting limpid mixture from the percolation step must have a 65 % ethanol concentration, which is confirmed using an alcoholmeter (Giannis 1991). The liquid phase obtained is then used to produce several products, some of which can be used as drops or further concentrated in a water bath to create concentrated extracts.

Hard gelatine capsules

Phytotherapy capsules use a hard gelatine shell for oral consumption. The hard gelatine capsules used are of animal origin, which means pork skin gelatine is used in the production of such capsules (Hafidz et al. 2011). The production of hard gelatine capsules starts with the preparation of the pork skin, which undergoes various stages where sulphuric acid and sodium hydroxide are used (Parker and Tyedmers 2012). After the preparation of the pork skin, metal moulds are dipped in the gelatine and cooled so that the gelatine starts to harden at the surface of the moulds. After the moulding step, the capsules are dried, through several drying stages, stripped off the moulds and trimmed to the required size (Pharmapproach 2021). The data for capsule production can be found in Sect. 2.6.

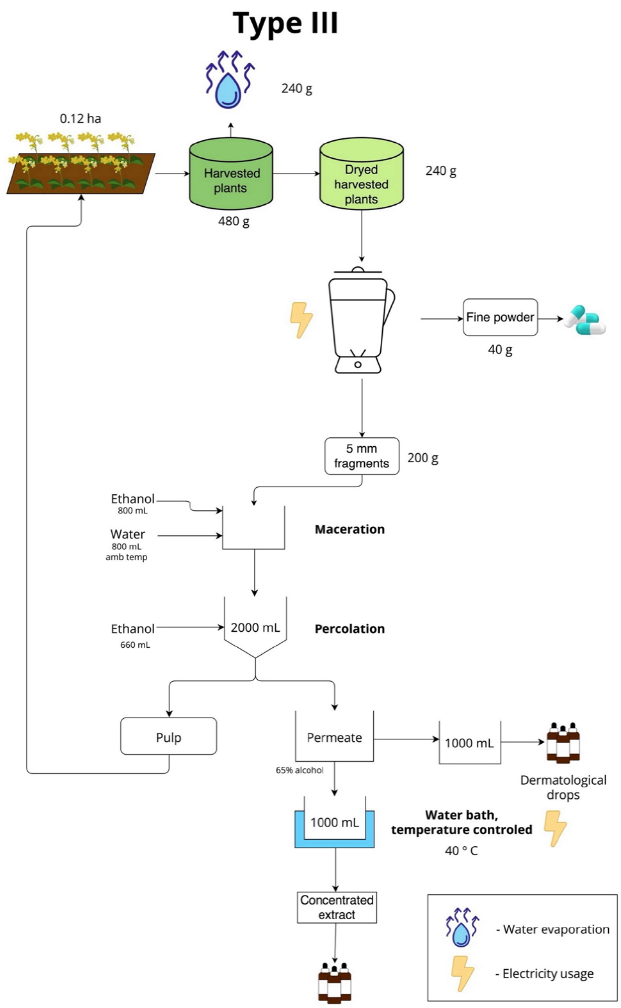

Fig. 4 Type III of the hydroethanolic extraction process

Table 1 Inventory (process inputs) of data used for the LCA modelling in SimaPro

	Unit	*Passiflora incarnata*	*Calendula officinalis*	*Vitex agnus-castus*
Inputs				
Dried plants	g	240	240	240
Ethanol	mL	1500	700	1200
Water	mL	800	1000	600
Electricity	kWh	1.31	0.7	1.4
Outputs				
Evaporated ethanol	mL	600	350	1000
Evaporated water	mL	450	450	450
Solid waste (pulp)	g	220	220	220
Oral drops (50 mL bottles)	U	20	20	20
Capsules (50 units packages)	U	2	2	–

The data presented is based on observations of the extraction processes

Glass bottles for oral drops

The oral drops are commercialised in brown glass dropper bottles with a plastic cap containing a glass pipette. The LCA of the manufacturing process of these bottles was not modelled due to a lack of available information. Nevertheless, the components of each bottle were weighed and considered for the LCA analysis. In this way, the impact of producing each material that comprises the bottle is considered, and only the manufacturing of the bottles themselves is neglected. The inventory of bottles used for the LCA analysis is listed in Sect. 2.6.

Life cycle inventory

Using very specific species of plants is challenging for the life cycle inventory determination, since the data on these plants can be scarce. Two databases, Agri-footprint (v4.0) and Ecoinvent 3 (v3.6), were utilised, using the latest available versions in SimaPro (Commission 2021); (The International Standards Organisation 2006); (Moreno-Ruiz et al. 2019).

Five products were the focus of this study, the phytotherapeutic capsules produced from each of the three plants studied, as previously mentioned. Oral drops and phytotherapeutic medicines where no hydroethanolic extraction was performed were also studied. For the analysis of phytotherapy capsules (with hydroethanolic extraction), the functional unit was considered to be a package of 50 phytotherapy capsules of the respective plant. For the oral drops, a bottle of 50 mL was considered the functional unit.

A total of 20 km was considered as the car transport required to produce the capsules, as the plants are produced locally, close to the pharmaceutical laboratory. Also, the pharmacy is less than 2 km away from the laboratory, so transportation between these two sites was not considered in this study.

The data presented in Tables 1 and 2 have been used for LCA modelling of new processes and materials in SimaPro, corresponding to those previously described in Sects. 2.1 through 2.5.

Life cycle impact assessment

The life cycle impact assessment (LCIA) of the hydroethanolic extraction processes and product assembly was performed in SimaPro (Herrmann and Moltesen 2015) using the Environmental Footprint 3.0 method (Commission et al. 2023). The primary focus of the analysis was the comparison of the single scores of each of the three phytotherapeutic capsules, with the most impactful sustainability impact

Table 2 LCI of the hard gelatine capsules, glass bottles and plastic containers used for the commercialisation of phytotherapeutic capsules and oral drops

Glass bottles			Reference
Input	Unit	Amount	
Brown glass	g	60	This work
White glass	g	10	
Polypropylene	g	20	
Plastic containers for the capsules			
Input	Unit	Amount	
High density polyethylene (HDPE)	g	30	This work
Hard gelatine capsules			
Input	Unit	Amount	
Pork skin	g	25.00	Parker and Tyedmers 2012))
Sulphuric acid	g	3.11	
Sodium hydroxide	g	5.27	
Electricity	kWh	0.04	

categories, namely land use, photochemical ozone formation (POF), and global warming potential (GWP), also being analysed. The resulting data obtained from SimaPro were further analysed and discussed.

Results

LCA of phytotherapeutic products from *Passiflora incarnata*, *Calendula officinalis*, and *Vitex agnus-castus* serves as a crucial analysis in evaluating the environmental impacts associated with the production of such products. In this section, the results of the LCA of 5 final products are presented: first, a comparison of the environmental impacts of 3 phytotherapeutic capsules; second, the environmental impact of *Passiflora incarnata* extract oral drops; and finally, an LCA analysis of phytotherapeutic capsules without hydroethanolic extraction.

Phytotherapeutic capsules from hydroethanolic extraction comparison

The processes of production of phytotherapeutic capsules made from several plants were assessed, and the single-score results are graphically represented in Fig. 5. As described in Sect. "Methodology" for the LCA of the production of phytotherapeutic capsules, the life cycle of each plant was considered, from the cultivated land until the "gate" of the pharmacy, where the analysis in this work stops. Each plant process is unique; however, every process utilises extraction at some point and ultimately leads to the production of phytotherapeutic capsules. It is possible to observe from the results in Fig. 5 that land use is the most significant contributor to the overall single score of each capsule. This recurrent pattern, irrespective of the plant species or extraction type employed, points to the inherent environmental cost of organic cultivation as the primary constraint in decreasing environmental impacts of phytotherapeutic production chains.

The single scores obtained for each product have very small values since in the assessment, the function unit considered is 50 capsules of the respective plant, which means that in the case of the *Passiflora incarnata*, a total extract of 5 g is being evaluated. Therefore, small overall impacts (the unit for the single scores in Fig. 5a is mPt) were to be expected. Even though small, the impacts can be evaluated and compared, determining the largest contributors to the overall impact, which, in the case of these three products, were determined to be land use (see the relative importance bar graph in Fig. 5b). The *Vitex agnus-castus* phytotherapeutic capsules have a lower environmental impact than the *Passiflora incarnata* ones, due to the maceration step

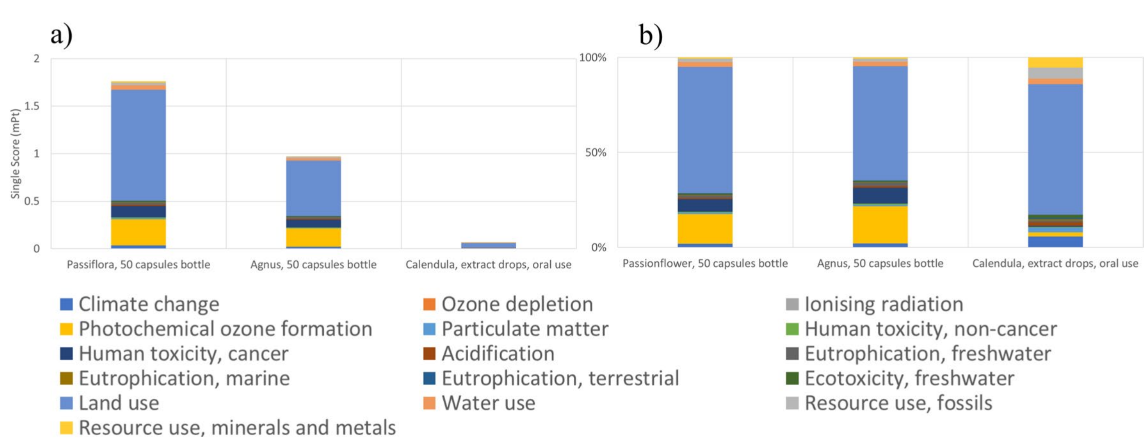

Fig. 5 Single-score results obtained for the *Passiflora incarnata* and *Vitex agnus-castus* capsules and *Calendula officinalis* drops. **a** Absolute single score, **b** relative single score

from hydroethanolic extraction of the active pharmaceutical ingredient (API) from *Vitex agnus-castus* being more efficient than that of *Passiflora incarnata*. This difference highlights that extraction process design (specifically the avoidance of ethanol in the maceration step) can meaningfully, albeit secondarily, differentiate the environmental profiles of otherwise comparable products.

The *Calendula officinalis* extract drops are a product that is different from the capsules produced from *Passiflora incarnata* and *Vitex agnus-castus;* however, these are also used in phytotherapeutic treatments, and the API is obtained through a hydroethanolic extract. This process has a significantly lower single score than the ones obtained for *Passiflora incarnata* or *Vitex agnus-castus. This* comes from the fact that for the drops from *Calendula officinalis* the extract for the product is obtained directly from the percolation step, without the need for further drying of the extract, so no emissions of ethanol or electricity usage for the water bath. This result suggests that product form (drops vs. capsules), by determining whether a drying step is required, can be a more impactful design decision than the choice of plant species itself when targeting reductions in the GWP impact category.

Even though the climate change impact category has a very small impact on the overall environmental evaluation, as shown in Fig. 5, the absolute values of this category are displayed in Table 3, where it is possible to observe once again that the *Calendula officinalis* extract drops have a significantly lower environmental impact, even in the climate change impact category. *Passiflora incarnata* and *Vitex agnus-castus* have a climate change impact in the same order of magnitude, which was to be expected since the processes used in the extraction of both release ethanol to the atmosphere; however, in different amounts. The 39 % lower GWP of the Vitex agnus-castus capsules (0.813 vs. 1.33 kg CO_2 eq) can be traced primarily to the ethanol-free maceration step, reinforcing that solvent use is the dominant driver of GWP within the extraction subsystem, even if it remains subordinate to land use at the system level.

In the following subsection, a closer examination of each process compared in Fig. 5 is presented, along with an analysis of the network of processes that leads to the production of these products.

Table 3 GWP impact category absolute values for each of the plants studied

Impact category	Product		
	Passiflora incarnata caps	*Vitex agnus-castus* caps	*Calendula officinalis* drops
GWP weighted (μPt)	34.52	21.15	4.015
GWP absolute (kg CO_2 eq)	1.33	0.813	0.154

Individual analysis of phytotherapeutic capsules

Passiflora incarnata

The process of production of *Passiflora incarnata* phytotherapeutic capsules has a significant impact on the land used. With the use of organic production methods, a half-hectare yields 10 kg of dried plants ready for extraction. This cannot be changed due to the intent of using organic methods for its production. However, there are steps in the production of the final product that might have room for improvement, i.e., minimisation of environmental impacts. In Fig. 6 it is possible to identify the most significant contributing processes to the environmental impact of *Passiflora incarnata* phytotherapeutic capsule production, with the processes of breeding, growing, and harvesting being the most impactful. The fact that these processes are the most impactful is also represented in Fig. 7, with the land use impact category being the most impactful one, which leads to a contribution of 66 % of the growing and harvesting process to the overall impact of the *Passiflora incarnata* capsules (see pie chart in Fig. 7b).

In Fig. 6 is also possible to observe that electricity is used in the processes of crushing and later in water boiling and water bath ("*Passiflora incarnata* extract, dried" block in Fig. 6), even though the electricity represents a small impact in the overall environmental impact, this impact can be further decreased if solar panels, or other clean energy source, were to be used. Since the electricity currently used is from the Greek power grid is 10 % produced from renewable sources (IEA, Greece 2024); (Ritchie et al. 2020). Given the already marginal contribution of electricity to the overall single score, however, this substitution would yield limited absolute gains, reinforcing that land use reduction remains the more impactful mitigation opportunity.

As stated for electricity, ethanol also has a significant environmental impact, as shown in Figs. 6 and 7, this is partially caused by the production of ethanol and from the ethanol emitted to the atmosphere. This is partially caused by the production of ethanol and by the ethanol emitted to the atmosphere. If the ethanol used for the maceration and percolation steps was to be replaced by bioethanol, with a carbon–neutral environmental impact, the impacts associated with the use of this solvent could be minimised. Nevertheless, as further discussed in Sect. 3.4, the contribution of ethanol to the overall single score remains secondary to land use, limiting the absolute environmental benefit of this substitution.

The high-density polyethylene (HDPE) bottles and the hard gelatine capsules, in which the *Passiflora incarnata*

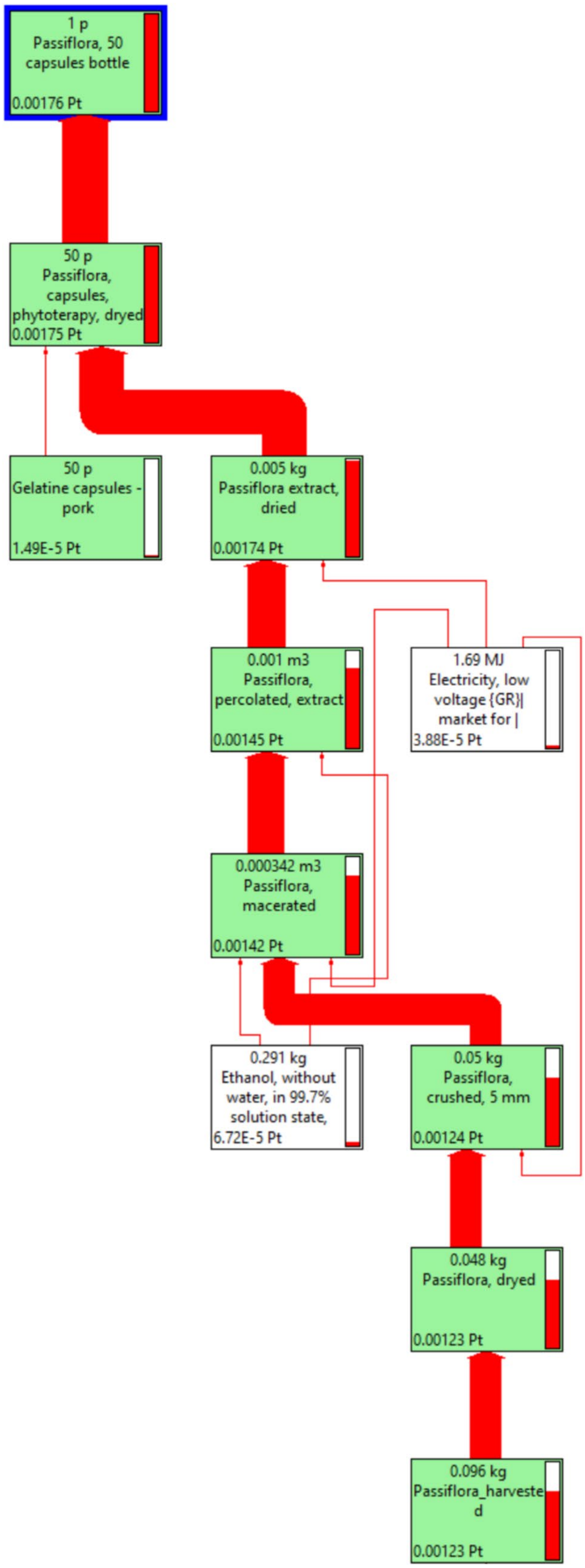

Fig. 6 Passiflora *incarnata* LCIA network obtained from SimaPro with a cut-off of 0.7 %

extract is consumed, were determined to have a very small to negligible impact on the overall environmental impact of the *Passiflora incarnata* capsules. In Fig. 7b it is possible to observe that HDPE bottles and the gelatine capsules have almost 0 % impact on the overall environmental impact, which was to be expected, since very small quantities of these materials are being used, a 30 g bottle and 50 hard gelatine capsules.

Vitex agnus-castus

The *Vitex agnus-castus* capsules have a similar environmental impact profile to the previously analysed *Passiflora incarnata* phytotherapeutic capsules. However, they have their own characteristics, with a lower overall impact, which leads to an increase in the relative importance of the impact of the bottle for example (see relative importance pie chart in Fig. 8b). Land use is the impact category with the largest contribution to the total environmental impact, which had already been seen in Fig. 5; however, in Fig. 8a is possible to observe that this impact category is an order of magnitude larger than every other impact category, except for photochemical ozone formation, which leads to a 60 % relative importance of the growing and harvesting processes to the overall environmental impact. This improvement further confirms that mitigation strategies targeting the extraction subsystem in isolation are insufficient to substantially reduce the total environmental impact of Vitex agnus-castus phytotherapeutic capsule production.

As described in Sect. 2.2, the maceration of the type III process used for the hydroethanolic extraction of *Vitex agnus-castus* does not use ethanol; instead, it uses boiling water to open the seeds. This leads to a small relative contribution of the maceration process to the overall impact of the *Vitex agnus-castus* phytotherapeutic capsules. The drying of the extract here takes a more significant role, accounting for 27 % of the overall impact. This can be mitigated if the released ethanol were to be captured. A transition to a cleaner energy source to power the water bath used, as well as a bio-derived ethanol, would represent at most an improvement of 6 % in the overall environmental impact.

Calendula officinalis

The *Calendula officinalis* phytotherapeutic capsules LCA results are graphically represented in Fig. 9a, where a similar distribution of environmental impacts is observed, similar to the two previously shown products. However, here there are different contributors to the overall impact of the *Calendula officinalis* extract drops, for example, the glass bottles represent 21 % of the impact of this product, yet the growing and harvesting are the processes with the largest contribution, with 69 %. The maceration step here has a contribution of

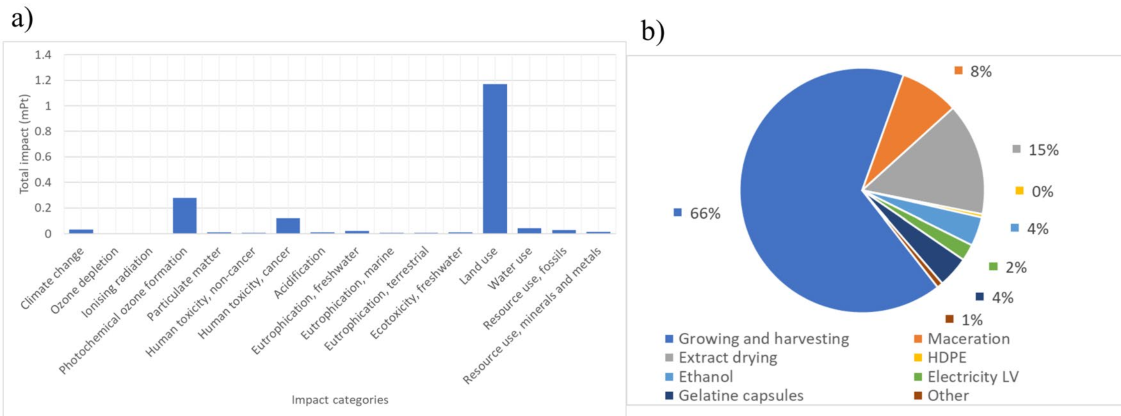

Fig. 7 Passiflora *incarnata* environmental impacts. On the left bar graph are the absolute values of each impact category, and on the right pie chart there is the relative impact of every process and material that make the *Passiflora incarnata* phytotherapeutic capsules

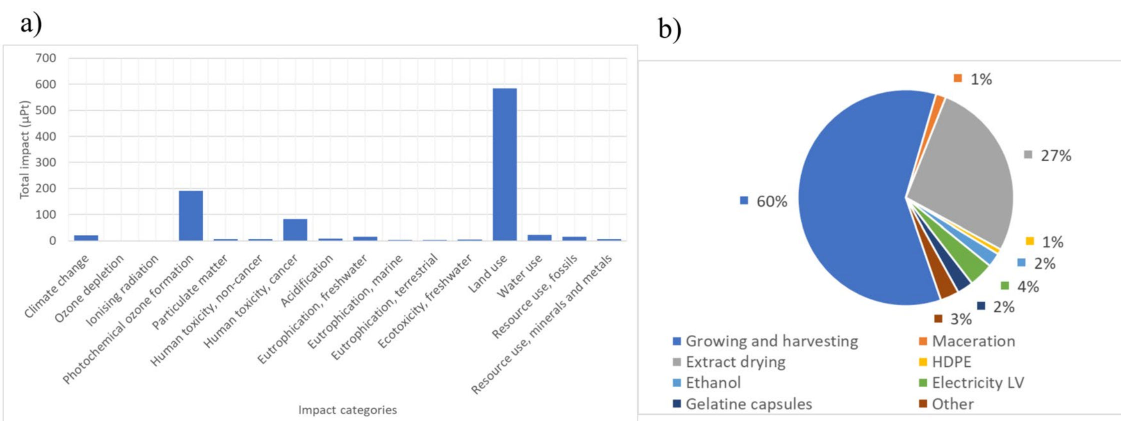

Fig. 8 *Vitex agnus-castus* environmental impacts; on the left bar graph are the absolute values of each impact category, and on the right pie chart is the relative impact of every process and material that makes the *Vitex agnus-castus* phytotherapeutic capsules

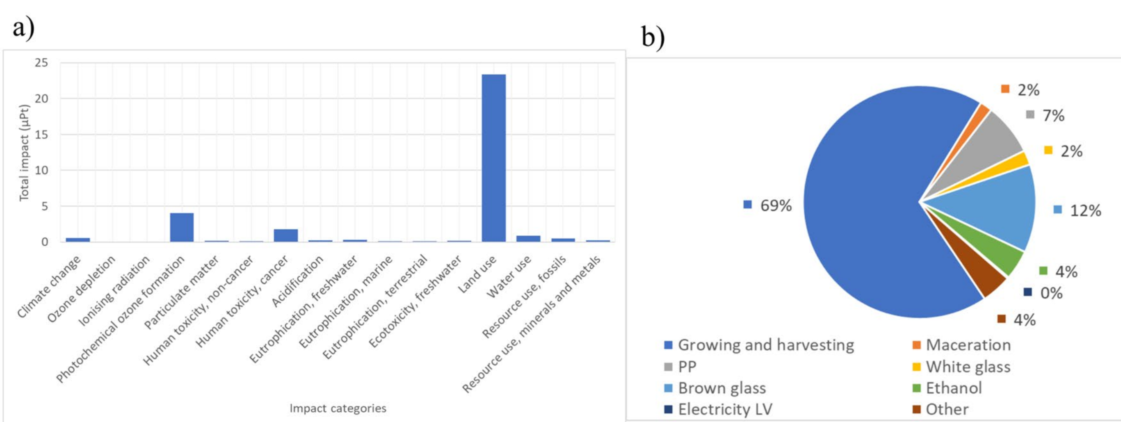

Fig. 9 Calendula *officinalis* environmental impacts results. The bar graph presents the absolute values of each impact category, and the pie chart presents the relative impact of every process and material that constitutes the *Calendula officinalis* hydroethanolic extraction to produce phytotherapeutic capsules

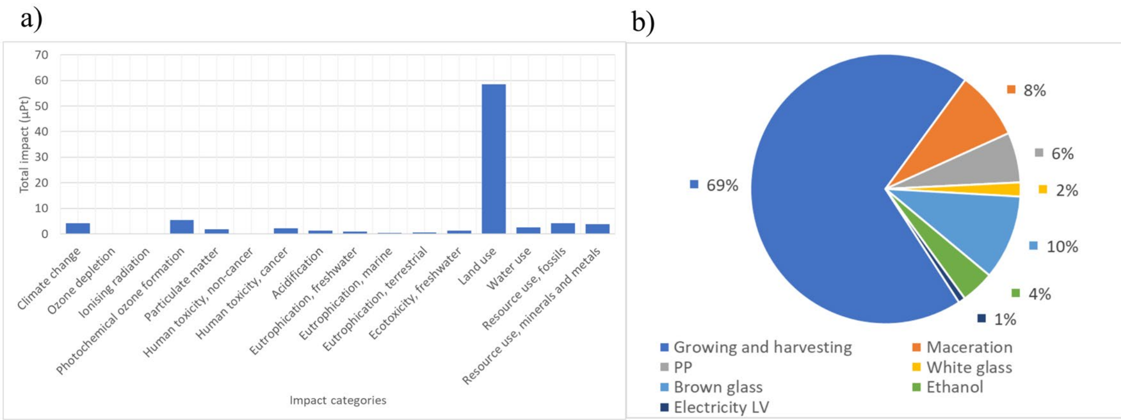

Fig. 10 Results for the oral drops of *Passiflora incarnata. The* bar graph presents the absolute values of each impact category, and the pie chart presents the relative impact of every process and material that constitutes the production of the oral drops and the bottles

just 2 %, which comes from the fact that equal amounts of water and ethanol are used in this step, and both are used at room temperature.

Even though the use of carbon–neutral energy tends to lead to improved environmental impacts, here the electricity represents nearly 0 % of the total impact of the *Calendula officinalis* drops; however, the ethanol consumed represents 4 % of the total impact. Therefore, the use of bioethanol would lead to a decrease in the overall environmental impact.

Oral drops

Oral drops can be made from each of the assessed plants in this study; however, here is presented just the LCA done to the *Passiflora incarnata* oral drops. In this model, all steps of the hydroethanolic extraction of the *Passiflora incarnata* extract were considered, as well as the glass bottles used for the final product (see description in Sect. 2.5). Even though the process of building the bottles was not considered, the materials for the construction of the bottle were.

From Fig. 10 it is possible to observe that the glass bottles have a small, yet significant, impact in the overall environmental impact of the oral drops from *Passiflora incarnata* (representing 18 % of the overall impact, white and brown glass and polypropylene). This comes from the fact that each bottle uses a small amount of glass, even though the glass industry is a high carbon emitting industry (Schmitz et al. 2011). The largest contributors to the overall impact are the growing and harvesting processes, accounting for 69 % of the overall impact. This comes from the fact that the land use impact category has an impact that is one order of magnitude larger than any other category. Comparing these results with the *Passiflora incarnata* phytotherapeutic capsules (Sect. "Individual analysis of phytotherapeutic capsules"), the omission of the drying step in the oral drops reduces the GWP contribution of the extraction subsystem but does not substantially alter the overall single score, since land use continues to dominate in both product forms. This finding demonstrates that formulation choices primarily affect secondary impact categories, not the principal environmental burden.

Phytotherapeutic capsules from *Passiflora incarnata* without hydroethanolic extraction

Phytotherapeutic capsules can be made directly from plants, i.e., no extraction is performed. In this section, the environmental impacts of producing phytotherapeutic capsules from *Passiflora incarnata* are presented. The production processes of these capsules were described in Sect. 2.4, where the plants are collected, dried, crushed, and encapsulated.

In Fig. 11 it is possible to observe that the land use is once again the main contributor to the overall environmental impact of this process. However, in this process there is almost no contribution to the climate change impact category, since there is no hydroethanolic extraction, there is no ethanol used and there is no boiling water added or water bath, therefore, the main contribution to the environmental impact comes from the land used for the cultivation of the plants and the hard gelatine capsules.

Sensitivity analysis

A sensitivity analysis was carried out on selected key parameters of the LCA models, by replacing certain SimaPro inputs with greener or alternative sources (such as renewable electricity mixes or bioethanol) to assess their individual effects on the overall environmental impacts and clarify the interpretation of the main findings.

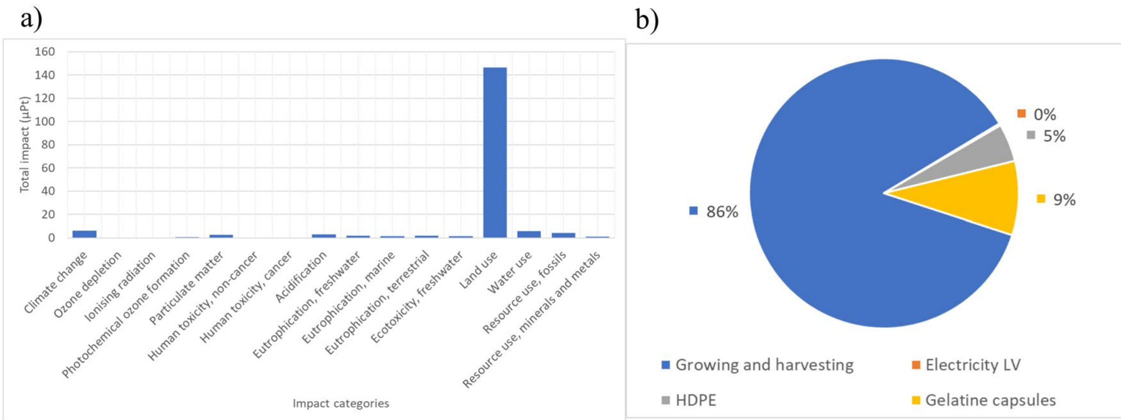

Fig. 11 Results for the phytotherapeutic capsules of *Passiflora incarnata* without hydroethanolic extraction. The bar graph presents the absolute values of each impact category, and the pie chart presents the relative impact of every process and material that constitute the production of phytotherapeutic *Passiflora incarnata* capsules

Land use

As land use was determined to be one of the most significant contributors to the overall impact of phytotherapeutic product production, a variation in the cultivated area was considered. If a more efficient cultivation method were used (Wittwer et al. 2021); (Purnhagen et al. 2021), reducing the area used by 50 %, 0.06 hectares would yield the same 480 g of harvested plants. This would lead to a 50 % decrease in land use and a 33 % reduction in single score. Therefore, this highlights the importance of land use in the overall impact. These results underscore the dominant role of land use in the assessed systems and the potential benefits of agricultural optimisation, even within organic production constraints. Consequently, engagement with precision agriculture or agroecological intensification programmes represents a substantially more impactful pathway to environmental improvement than any of the solvent or energy substitutions explored in the remainder of this sensitivity analysis (You et al. 2024).

Electricity sources

As mentioned before, the electricity used comes from the Greek power grid. If a local renewable production of electricity were used (photovoltaics, for example), the impacts associated with electricity consumption would be significantly reduced. This effect, the LCA models were recalculated by replacing the Greek grid mix with three alternative renewable options: photovoltaics, wind power, and biomass-based electricity. In the SimaPro modelling, the foreground electricity inputs were substituted by each renewable option, and the resulting environmental impacts for all assessed products were obtained. Under these scenarios, the use of renewable electricity would lead to an approximate 30 % reduction in climate change impacts, a 50 % reduction in ozone depletion, and a 75 % reduction in freshwater eutrophication.

Ethanol versus bioethanol

Ethanol is used across all extraction processes considered, with varying quantities that influence the overall environmental impacts of each product. Although bioethanol production carries associated environmental burdens (e.g., agricultural inputs and processing energy), these are typically lower than those of conventional fossil-based ethanol for key categories like climate change, making it a candidate for substitution. To quantify this potential without implying carbon neutrality, a sensitivity analysis replaced fossil ethanol with bioethanol from fermentation. The results showed a net 4 % increase in the overall single score—driven by deteriorations in other indicators (e.g., land use, eutrophication)—that offset the 2 % climate change improvement, illustrating realistic trade-offs in material sourcing decisions.

Conclusions

In this work, three hydroethanolic extraction processes were studied using life cycle assessment. The processes mainly differ in the quantities of solvents used and in the temperatures at which solvents are used. Resulting from these three types of process, five products were evaluated: phytotherapeutic capsules of *Passiflora incarnata* and *Vitex agnus-castus*; two types of drops, dermatological and oral from *Calendula officinalis* and *Passiflora incarnata*, respectively; and phytotherapeutic capsules from *Passiflora incarnata* without the hydroethanolic extraction. The phytotherapeutic capsules of *Passiflora incarnata* and *Calendula officinalis*, as well as the dermatological drops of *Calendula officinalis*, were the focus of this work, and the LCA analysis revealed that the *Passiflora incarnata* capsules had the most significant environmental impact (in terms of single score) of these three products.

For each product, land use was found to be the most impactful category, as expected, given the low crop yields obtained from such a large portion of the land. The processes studied have the greatest room for improvement in this category, so improving the way the land is currently farmed is highly recommended, with improved farming techniques, but this must be done while ensuring that the organic style of production is maintained.

Another category that has a significant impact on the overall environmental assessment is Photochemical Ozone Formation (POF), since the three processes evaluated inherently result in the emission of ethanol, which is one of the most potent non-methane volatile organic compounds (the unit of measurement for this category). The phytotherapeutic capsules of *Passiflora incarnata* were found to have the greatest environmental impact in the POF category, primarily due to the type of process used, which emits the greatest amount of ethanol (see Table 1). This result highlights that, when land use impacts are comparable across products, the extraction solvent system becomes the decisive differentiator in the overall environmental profile. This impact can be mitigated by implementing ethanol capture technology, which could significantly reduce or eliminate the amount of ethanol emitted into the atmosphere.

In terms of climate change potential, all the studied products have a small impact in this category, which was to be expected since there are no direct carbon emissions (except for the ethanol emissions and transportation). Once again, *Passiflora incarnata* capsules were found to have the most significant impact in this category, with 1.33 kg of CO_2 equivalents emitted for every 50 capsules produced and packaged.

Electricity was found to be a very small contributor to the environmental impact of each product, less than 2 % in each case. However, even if small, there is some margin for sustainable development in the production of such products. This impact can be substantially eliminated if a clean energy source is used instead of the Greek power grid.

The use of bioethanol is strongly encouraged, as ethanol accounts for no more than 4 % of the environmental impact of a product, and carbon–neutral ethanol, coupled with ethanol capture as mentioned above, would result in a lower overall environmental impact.

Overall, the five products were found to have a low environmental impact, as the products are mostly derived from plants. Notably, the comparison between extracted and non-extracted Passiflora incarnata capsules reveals that the hydroethanolic extraction step is almost entirely responsible for the GWP and POF contributions, while leaving the dominant land use burden unchanged, a finding with direct implications for the prioritisation of improvement strategies. However, there is room for improvement in the way these plants are grown, allowing for a reduced land use impact. The contributions to the POF and climate change indicators from all products can be reduced, as these are the most direct impacts of the production of such products.

The research presented in this study was developed under the close supervision of experienced phytotherapeutic pharmaceutical practitioners. Nevertheless, several extraction steps are carried out empirically, relying on practitioner expertise rather than precisely controlled parameters, which introduce uncertainty in the inventory data. The main shortcomings of this work lie in the fact that the plants used were not in the available databases, and some assumptions were made. Future work should focus on reducing inventory uncertainty through controlled experimental measurements, extending the system boundary to include end-of-life packaging, and incorporating an economic assessment to contextualise the environmental trade-offs identified here.

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Author contributions RD did the data acquisition, data curataion, representation and wrote the main manuscrip text. HM was responsible for the funding, data curation, writing and reviewing the manuscript. SS was responsible for reviewing the manuscript and make the data available.

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Data availability The data associated with this study has not been made available in any repository, yet it can be made available upon request.

Declarations

Conflict of interest The authors declare that they have no known conflict of financial interest or personal relationships that could have appeared to influence the work reported in this paper.

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