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▶ **To cite this version:**

Farid Chemat, Maryline Abert-Vian, Anne-Sylvie Fabiano-Tixier, Jochen Strube, Lukas Uhlenbrock, et al.. Green extraction of natural products. Origins, current status, and future challenges. Trends in Analytical Chemistry, 2019, 118, pp.248-263. 10.1016/j.trac.2019.05.037 . hal-02625657

HAL Id: hal-02625657

https://hal.inrae.fr/hal-02625657v1

Submitted on 25 Oct 2021

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Version of Record: https://www.sciencedirect.com/science/article/pii/S0165993619300706
Manuscript_829254b1bcebd174e1d50d90d4a5633a

Green extraction of Natural Products.
Origins, Current Status, and Future Challenges

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Abstract

Green extraction of natural products is based on design of extraction processes which will reduce or eliminate energy consumption and petroleum solvents, while ensuring a safe extract and quality. It is a concept to meet the challenges of the 21st century protecting both our environment and consumers, and in the meantime, enhance competition of academia and industries to be more ecologic, economic and innovative. This review will present definition, principles and current status of green extraction. We will discuss future challenges with applications in the agro-food sectors, cosmetics and perfumery, biofuels and fine chemicals.

Key words: Green extraction; intensification; bio-based solvents; bio-refinery; natural products.

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Abreviations

CEO : citrus essential oil

CM: conventional maceration

CMR: Carcinogenic, mutagenic and reprotoxic

DIC: instant controlled pressure drop

EO: essential oil

EVOO: Extra-virgin olive oil

HD: hydro-distillation

IEA: International Energy Agency

LCA: Life cycle Assessment

LCI: Life cycle inventory

MAE: microwave assisted extraction

MHG: microwave hydro-diffusion and gravity

MW: microwave heating

OMWW: Olive mill waste waters

OPW: orange peel waste

OTPB: Olive tree pruning biomass

PLE: pressurized liquid extraction

SCE: Supercritical CO2 extraction

SWE: Subcritical water extraction

TPC: Total Phenolic content

UAE: Ultrasound-assisted extraction

US: Ultrasound

VOC: Volatile Organic Compounds

1. Introduction

Until the start of the petroleum era plant-derived biomass was the main source of reagents, ingredients and products for food and non-food applications. The spectacular growth of petroleum-based processes led to a withdrawal from those based on biomass. However, the depletion of fossil resources, upon which the current International industry and economy heavily depends, and environmental considerations force us towards a post-petroleum society. While green chemistry [1-2] has given rules for modern chemistry, green extraction of natural products [3-5] could be one of the solutions from the past to the future of humanity as an ecologic and an economic chemistry, and turning to “Green Chemistry of Natural Products”.

Natural extracts can be sourced in huge number of plants materials and includes primary and secondary metabolites as proteins, fats and oils, dietary fibers, sugars, antioxidants, essential oils and aromas, and colors. They are largely used as ingredients in the food processing industry for their texturing, preservative or coloring properties, and as active compounds in cosmetics or pharmaceuticals. Conventionally, such extracts are obtained using solid-liquid extraction considered as a unit operation. Extraction process is composed of several unit operations such as pre-treatment of plant material (drying, grinding…) and post-treatment of liquid extract (filtration, concentration, purification…). The most crucial unit operation in the process is solid-liquid extraction, particularly when it is not optimized, is often time and energy consuming, induces the use of huge amount of water or petroleum solvents harmful for environment and users and generates large quantity of waste. Moreover, resulting extract is not always safe as it may contain residual solvents, contaminants from raw material, or denatured compounds due to drastic extraction conditions [6-7].

In this context, extraction specialists aimed in a first time to intensify their processes. The objective is to obtain higher extraction efficiency and higher quality extract while reducing extraction time, number of unit operations, global energy consumption, quantity of solvent in the process, environmental impact, economical costs and quantity of waste generated. In the last decades, with the increasing interest to environmental, economic and safety considerations, innovative alternatives with durable and green values have been hugely implemented in food processing, cosmetic and pharmaceutical industries. It was particularly initiated by the publication of the twelve principles of green chemistry [1] and the twelve principles of green engineering [2] which define the good practices to be adopted. Following these principles, researchers from academia and industry define the term of “green extraction” and establish the six principles of green extraction [3]. These principles intend to act on the main inputs and outputs regarding a global extraction process (Figure 1).

Green extraction is based on the discovery and design of extraction processes which will reduce energy consumption, allows use of alternative solvents and renewable natural products, and ensure a safe and high quality extract/product". In this definition, the main idea of intensification is identified. The listing of green extraction principles was established to guide researchers from academia and industry in their demarche towards green innovation, not only regarding the process, but in all aspects of solid-liquid extraction.

In this review, good practices guidelines regarding each principle are developed. Examples of success stories are presented in order to show the potential and the feasibility of such practices at different scales. Proposed success stories show that the adoption of such demarche is possible at laboratory and industrial levels. Green extraction concept and principles have been identified and described not as rules but more as innovative examples to follow, discovered by scientists and successfully applied by academia and industry.

2. Principle 1: Innovation by selection of varieties and use of renewable plant resources.

2.1. Context

The increasing demand of natural products and extracts to answer the needs of food, cosmetic and pharmaceutic industries is leading to the over-exploitation of natural plant resources. Producers of natural extracts have to consider other issues, such as respect for the environment and human health or production with high yields, which are sustainable key issues for industrials. History reports several examples of plant extinction because of over-utilization. More particularly, the large-scale uncontrolled harvesting of natural resources may carry the risk of making the species rare or even extinct. The preservation of biodiversity is therefore mandatory in the respect of future generations. In the context of green extraction, the use of renewable resources, plant breeding or the use of ingenious biotechnological processes are many approaches to consider in order to avoid the extinction of endemic species.

2.2. Good practices guidelines

To limit the impact of industrial processes on the environment and to produce products that meet the values of green extraction, plant cultivation stage has to be in accordance with good practices :

- Integrate the raw material to an ecosystem vision including a social/ societal, environmental and economic diagnosis,
- Rely on standards such as ISO 26000, which was developed to provide guidance on how to behave in a socially responsible way,

- Implement protocols to promote the performance of the resource by plant breeding. Plant breeding approach involves increasing yields, producing varieties containing particular target compounds or select varieties adapted to region and climate,
- Support treatment technologies that (i) enable efficient production of crops and crop protection products (ii) meet the demands of an agriculture friendlier to environment and workers with varieties resistant to pests and pathogens,
- Avoid cultures generating pollution, threatening biodiversity and competing with local vegetation or local food crops,
- Better manage and develop the inputs during cultivation (water, pesticides and fertilizers).

2.3. Success stories

2.3.1. Towards renewable resources

Currently, most medicines are extracted from plants. The anti-cancer paclitaxel (Taxol®) extracted from the bark of the western Yew (*Taxus brevifolia*) is the best-known example. During the 1970's, no less than 30 tons of bark were collected for clinical trials, considering that 10 kg of dry bark produce only 1 g of taxol after extraction and purification. These low yields resulted in an over-exploitation of trees; however, due to the complexity of the molecule of interest, a synthetic way was not economically viable. In this context, a large number of research projects have been aimed at finding alternatives to felling trees of this threatened species. In 1980, 10-deacetylbaccatin III (10-DAB III), which shared the same tetracyclic framework as that of paclitaxel, was identified as a plausible starting material for the semi-synthesis of paclitaxel. The French research group of Pierre Potier [8] had shown the feasibility to isolate relatively large quantities of 10-DAB III from the leaves of European Yew, which is renewable source as opposed to the bark of the Pacific Yew (*Taxus brevifolia*).

2.3.2. Plant breeding and plant cultivation in response to over-exploitation

In many vegetable crops, breeding programs have been devoted to improving yield, resistance to diseases, end-use quality and environmental performance [9]. Given the increased demand by consumers for plant-derived products with higher content in bioactive compounds, researchers and breeders are developing new knowledge and tools for an efficient breeding of the content in bioactive compounds in plants [10]. A big effort is running in the natural selection of varieties with much higher concentrations of active compounds as the example of the production of artemisinin [11]. Artemisinin, a sesquiterpene lactone, is known as an anti-malarial substance isolated from the herb *Artemisia annua* L., originating from Asia.

The extraction from *A. annua* leaves remains the only source of artemisinin ranging from 0.01 to 0.8% of the plant dry weight, makes artemisinin relatively expensive and difficult to meet a very high demand. Efforts have been made for breeding cultivars of the plant for higher artemisinin production. Currently-used plants produce around 1%.

Hypericum Perforatum (St. John's Wort) is an anti-depressant herb that is commonly used for its neurological effects. This herb is a rich source of flavonoids but also contains hypericins, tannins, hyperforins, phenolic acids and terpenoids and it is ranked among the ten top best-selling botanicals in U.S. The economic interest of this plant has stimulated the development of programs aimed at the selection and cultivation of improved cultivars of *H. perforatum* in Europe and North America [12].

Medicinal plants play a major role in the field of medicines and their over-exploitation often leads to their extinction. Favoring the sustainable cultivation of these species rather than wild harvesting would allow the preservation of biodiversity and meet the demand of a growing market. *Prunus africana* is an evergreen tree that grows in African mountains. Its products have been used for generations in African traditional medicine to treat prostate cancer. Generally, methods of exploitation are unsustainable; whole trees are debarked from the roots to branches or cut down prior to debarking, thus resulting to the death of trees. Today, *Prunus africana* is considered vulnerable and over-exploitation is regarded as the main threat to the species. Due to threats faced by this species, many programs have been in place for the purpose of encouraging direct regeneration, environmental education and by promoting sustainable harvesting practices. Cultivation of *P. africana* has been suggested as a possible solution to the current over-harvest of the species from the wild [13]. *Podophyllum hexandrum*, a Himalayan medicinal plant, is known for valuable drug podophylotoxin which is effective against many cancers. Due to its high demand and unskilled overexploitation, *P. hexandrum* is becoming rare and is in danger of extinction. Cultivation of this species may answer the growing needs for plant material [14].

2.3.3. Development of new technologies: Example of Plant milking

A new sustainable sourcing solution known as “plant milking” was developed by Plant Advanced Technologies for the production and extraction of substances of interest, preventing the destruction of plant material [15]. These plants are grown in a greenhouse in liquid medium. Actually, secretion and exuding of targeted substances through the roots in the culture medium are triggered by physical, chemical or biological stimulation These substances are then collected by standard extraction and purification methods. This process is particularly performed to produce active principles from rare plants, whose chemical synthesis is difficult and costly. Therefore, “plant milking” appears as an extraction way that respects biodiversity.

For example, such process enabled the production of, among others, tropane alkaloids of pharmaceutical interest from *Datura innoxia*. In this case, harvesting yields of three times more secondary metabolites were obtained in one year compared to an equal area of field-grown plants. Good results were also obtained with garden rue (*Ruta graveolens*) which contains furocoumarins (substances used to treat eczema and psoriasis), and with edelweiss, rich in antioxidants.

3. Principle 2: Use of alternative solvents and principally water or agro-solvents.

3.1. Context

In typical extraction and separation processes, large quantities of organic solvents are used [16]. Even though organic solvents have well-known advantages, their replacement with greener alternatives is necessary due to their toxic effects on the human health and the environment. Large part of these solvents is characterized as Volatile Organic Compounds (VOCs) that contributes to increase the risks of fire and explosion. Moreover, these solvents are easily released in the atmosphere and can act as air pollutants promoting the global warming [17]. Thus, a growing research area in green technologies is focused on development of environmentally friendly bio-based effective solvents which could meet both technological and economical demands (Figure 2). The use reduction of hazardous solvents is also one of the priorities of EU environmental policy and legislation for 2010 – 2050 period [18].

3.2. Good practices guidelines

The choice of the solvent is crucial in the demarche of green extraction. It must particularly ensure the durability of global process. To this end, good practices guidelines must be respected:

- Evaluation of a potential “solvent-free” alternative
- Use of 100 % natural, natural origin, renewable or agro-sourced solvent with condition of having good knowledge, evaluation and control of potential related risks
- Avoid the use of solvent which might affect the safety and health of operators and consumers: it must not be CMR or toxic; not induce allergenic effect and not endocrine disruptors.
- Use of solvent suitable with industrial facilities
- Prefer a solvent with high rate of recyclability (high bio-degradability and no bio-accumulation) to limit global process impact on environment
- Use of solvent with low VOC (Volatile Organic Compounds) emissions related
- Use of solvent which limit energy consumption and cost of global process.
- Ensure a maximal solvent recovery at the end of the process using various available techniques.

3.3. Success stories

3.3.1. Solvent-free extraction

Keeping in mind all these aspects, the application of solvent-free extraction processes is of great interest. The benefits of solvent-free conditions are evident: (i) avoiding costs and risks of large volumes of solvent; (ii) facilitated scaling-up; (iii) increased extract purity; (iv) enhanced safety due to reducing risks of overpressure and explosions [17]. Moreover, these methods shorten extraction time from hours to minutes, because solvent distillation, the bottleneck in work-up processes, is missing. It eliminates wastewater post-treatment and consumes only a fraction of the energy normally used in a conventional solvent-solid extraction method. Different enabling techniques, such as microwave hydrodiffusion and gravity (MHG), instantaneous controlled pressure drop, and pulsed electric field have been developed and successfully applied for solvent-free extraction of various valuable natural products (essential oils, aromas, edible oils, antioxidants, and other organic compounds) [19].

MHG technique developed in 2008 by Chemat et al. [20] exploits *in situ* dielectric heating on pant cells water causing the structure stretching leading to membrane and wall ruptures. In this way primary and secondary metabolites and cells water are collected from plant material. The described phenomena is called hydrodiffusion. Diffused components are then dropped by gravity into a continuous condensation system through perforated Pyrex disk [21]. MHG was applied in lab- and industrial-scale extraction of pigments, aroma components, and antioxidants from various natural sources [17].

3.3.2. Water, steam and sub-critical water

The greenest solvent seems to be water because non-toxic, non-corrosive, non-flammable, environmentally benign, naturally abundant, and available at low cost [22]. Still, water has some drawbacks which limit its use as universal sustainable solvent for extraction processes, such as low apolar compounds solubility and high energy consumption required to concentrate the product.

Water is in the supercritical state at temperatures above 374 °C and pressures above 221 bar [22]. In temperature range between 100 °C and the critical temperature, water is called subcritical, near-critical or pressurized hot water [23]. It shows many advantages with regard to extraction efficiency and selectivity [22]. Decrease in permittivity, an increase in the diffusion rate and a decrease in the viscosity and surface tension is noticed as the temperature increases [24]. In spite of the improvement in all these properties, the most important effect of the water temperature increase is undoubtedly the weakening of hydrogen bonds, resulting in a lower dielectric constant [25]. Hence, more polar target compounds with high solubility in water at ambient conditions are extracted most efficiently at lower temperatures, whereas moderately polar and non-polar targets require a less polar medium which is induced by elevated temperature [24].

It is known that water is an efficient solvent for extraction of polysaccharides even at the room temperature. Nevertheless, the extraction can be enabled using microwave irradiation (MW). This technique has been reported to be efficient for a variety of matrices including corn pericarp, wheat bran, flax shives, tamarind kernel, mulberry leaves, brewers' spent grain, watermelon rinds, tea flower, mushrooms, or traditional Chinese medicinal plants [22]. Water as a solvent has been applied also in ultrasound-assisted extraction (UAE). Pingret et al. [26] performed lab- and pilot-scale UAE extraction of polyphenols from apple pomace. A comparison showed that the total phenolic content (TPC) obtained by UAE was 30% higher than the content obtained by conventional extraction and with stronger antioxidant activity [26].

Due to its properties and thanks to the fact that water is easily available, safe, non-toxic, non-flammable, and environmentally friendly, the number of studies on the possibility of subcritical water application for the extraction of various compounds is constantly increasing. Up to date, subcritical water extraction (SWE) has been successfully applied for the extraction of antioxidants (phenols and flavonoids), essential oils, fatty acids, oils, carotenoids, sugars, mannitol, pectin, resorcinol, etc. [18]. Usually, extraction temperatures of 80-150°C and extraction times of 1-60 min have been used in SWE of phenols. However, optimal extraction conditions greatly vary, depending on the type of phenolic compound to be extracted. For example, in order to extract extremely labile polyphenols (e.g., anthocyanins), generally a lower extraction temperature is required (Table 1) [18, 23].

SWE setup typically consists of a solvent reservoir with a high-pressure pump for the water input into the system, a cell or column within an oven where the extraction occurs and a valve that maintains the pressure within the system [36]. In addition, the SWE and extraction with water under boiling point can also be performed using MW energy. The MW-assisted extraction (MAE) can be performed in: (i) pressurized reactors, under controlled temperature in a pressure closed vessels in which the solvent is heated above its boiling point or (ii) open-systems at atmospheric pressure. Closed systems are alternatively applied for SWE. MAE with water as solvent has been proposed to improve extraction yields [22]. Brahim et al. [37] applied MAE for polyphenolics from grape red marc, grape white marc and grape pomace in water (60–120 °C) and compared it to conventional methods. MAE gave significantly higher yields as compared to traditional extraction [37]. Coelho et al. [38] performed MW-assisted SWE for extraction of arabinoxylans and arabinoxylo-oligosaccharides from brewers' spent grain. The carbohydrates yield increased with the increase of the temperature in the range from 140 to 210 °C, during 2 min [38]. SWE has also been employed by Sixt et al. for the extraction of 10-DAB III from *taxus baccata* L. and artemisinin from *artemisia annua* L, substituting conventional solvent extraction [39, 40].

Compared to classic hydrodistillation, SWE showed several advantages in essential oil extraction [16]. High temperatures and long distillation times can induce modifications and losses of volatiles and high energy and solvent consumption [22]. Compared to classic hydrodistillation, SWE showed several advantages in essential oil extraction such are much shorter extraction time, lower costs and enhanced purity of the final product [16]. Khajenoori et al. [41] performed SWE of *Matricaria Chamomilla* L. essential oils and compared it to hydrodistillation. Products obtained by SWE resulted in more valuable essential oil as regard the oxygenated components. Moreover, the time of the extraction was shorter [41].

Water steam is widely used for the extraction of essential oils. It is based on the same principle of hydrodistillation, just there is no direct contact of matrix with water. The drawback of the essential oil extraction using steam is a long extraction time which can causes degradation of thermolabile compounds [42]. Fast and efficient extractions with water steam can be exploited in microwave steam diffusion and microwave steam distillation [43]. Moreover, these techniques offer simplified manipulation, reduced solvent consumption and lower energy input [44]. Both of these techniques were tested by Périno-Issartier et al. [43] for extraction of lavender essential oil and compared with conventional hydrodistillation method. This methods have shown to be very effective – the obtained extract had excellent quality and the extraction time was significantly shorter [43].

3.3.3. **Supercritical CO_2**

Supercritical CO_2 can be considered the ideal supercritical fluid thanks to its low critical constant (T_c=31.1 °C, P_c=7.38 MPa) and inert nature. It is non-toxic, non-explosive, inexpensive, readily available, is easy removable from the final product and it has a good extraction capacity due to its higher penetration power. Moreover, CO_2 is also generally recognized as a safe (GRAS) solvent.

Supercritical CO_2 is an apolar solvent and therefore it can be used for the extraction of weakly polar compounds with low molecular weight such as carotenoids, triglycerides, fatty acids, aromas etc. [18]. However, its low polarity makes it unsuitable for extraction of polar compounds such as pharmaceuticals and nutraceuticals, which is its biggest disadvantage. This limitation can be overcome by using polar co-modifiers [45]. Ethanol and methanol are the most widely used co-modifiers for the extraction of biologically active compounds [18]. Garmus et al. studied the extraction of phenolic compounds from pitanga leaves (*Eugenia uniflora* L.) using supercritical CO_2, and ethanol-water as co-modifiers, coupled with sequential extraction in fixed bed extractor. This method was compared with conventional extraction method (heating and stirring) using ethanol and water. Supercritical CO_2 extraction (SCE) showed to be much more effective – obtained extract that has a high extraction yield and high concentration of phenolic compounds of interest [46].

SCE has several large scale industrial applications, such as production of food (decaffeination of coffee and tea), food ingredients (hops and aromas, colorants, vitamin-rich extracts, ect.), nutraceuticals/ phytopharmaceuticals and removal of pesticides from rice [18]. This technology was also applied for extraction of oils from seeds, fruits, leaves and flowers, which are further used in food, pharmaceutical and cosmetic industry [47].

3.3.4. Glycerol

In biodiesel production, glycerol is generated as a co-product and it represents approximately 10% (w/w) of total output. In 2007 it was proposed as a green solvent [48]. Dooring the past decade it drawn a lot of attention in the field of organic chemistry due to its low price, attractive chemical properties (high polarity, ability to form strong hydrogen bonds and to dissolve a variety of organic and inorganic compounds), and promising physical properties (negligible vapour pressure, stability under typical storage conditions). Moreover, it is biodegradable, non-flammable and non-toxic [16]. However, glycerol as a solvent has a number of disadvantages. The most well-known disadvantage is its high viscosity. Still, this problem can be solved by heating above 60 °C or by using co-solvents [49].

Shehata et al. [50] studied the polyphenols extraction from two Artemisia species using heated water/glycerol mixture. The extraction provided very satisfactory yields in total polyphenols with glycerol concentration up to 90% (w/v) [50].

Apostolakis et al. [51] optimised polyphenol extraction from olive leaves using heated water/glycerol mixtures and compared the polyphenols yield with ethanol/water mixture. It was demonstrated that the heated aqueous glycerol solution is more efficient as compared with a hydroalcoholic solution in extracting olive leaf polyphenols. This procedure is preferable for the industrial application since the production cost would be significantly lower for two reasons: (i) extracts prepared in aqueous glycerol can be directly added into foods, supplements and cosmetics, as there is no necessity for further residual solvent removal, and (ii) there is no generation of waste or residual solvent. Furthermore, glycerol recycling and/or reuse is possible [51].

3.3.5. Limonene

Limonene, a cyclic monoterpene, is the major component of the citrus fruit skins essential oils (CEO) [53, 53]. Two optical isomers are present in CEO (D- and L-limonene), however, D-limonene makes 90 % of total CEO limonene [52]. The orange juice industry, that produces more than 50 million tons of fruit skin annually, represents a useful source for D-limonene and a challenging research field for the by-products valorisation. D-limonene is considered as a GRAS material by the U.S. Food and Drug Administration.

Different authors have indicated the high suitability of this molecule as a solvent for the extraction of natural compounds in order to replace petroleum-based solvents such as *n*-hexane and toluene [53, 54]. In 2008, Virot et al. [55] first described the use of d-limonene instead of *n*-hexane in the extraction of fats and oils in food using an efficient combination of microwave-integrated Soxhlet extraction and solvent removal through microwave Clevenger distillation. Analysed oils obtained from olive seeds via conventional heating (with n-hexane) and microwave Soxhlet extraction with d-limonene showed no significant difference [55]. Bermejo et al. [56] performed the extractions of thymol, the main monoterpene phenol found in thyme essential oil, using ethanol, limonene and ethyl lactate as solvents. The extraction temperatures tested were 60, 130 and 200 °C. The highest concentration of thymol in the extracts was obtained with limonene at the lowest temperature tested (60 °C). Moreover, regardless of the temperature applied, extraction with limonene provided higher concentrations of thymol in the extracts [56].

4. Principle 3: Reduction of energy consumption by energy recovery and using innovative technologies.

4.1. Context

Energy consumption is one of the major concerns of current industries, whatever sector of activity. It can be related to environmental issues, increased production costs and consequently loss of profitability. In this context, the new challenge of most industrials is to understand energy requirements of their processes, in order to minimize energetic input and favor recycling.

Among the most energy-intensive industries, 26 % belong to chemistry and plastics manufacturing and 16 % to food processing sector. Plant extraction field could be included in these two categories; there is a direct interest to optimize extraction processes in terms of energy efficiency. Moreover, traditional extraction processes such as distillation are well-known to be energy-consuming, which opens up many energy optimization possibilities.

Generally, energy consumption related to extraction processes can be reduced adopting four main approaches: optimizing existing process; recovering the energy released during the process;

assisting existing processes, particularly with innovative technologies; and using innovative processes.

4.2. Good practices guidelines

In the demarche of green extraction, the decrease of energy consumption can be achieved using different strategies:

- Focus on "low-energy" processes:
  - Conception of processes minimizing as far as possible energy consumption: extraction at ambient temperature, concentration with reduced pressure…
  - Optimization of existing processes, particularly extraction time and solvent consumption
  - Development of innovative processes with high energetic efficiency
  - Combining existing processes with new technologies
  - Development of intensified continuous processes
  - Optimization of energetic resources limiting energy waste and favoring energy recovery and reuse
  - Use of Life Cycle Assessment (LCA) demarche and digital twins based on physico-chemical process models as decision tool to compare different processes in terms of energy and improve energy performance ("eco-conception")
- Optimized management of:
  - Water (recycling, recovery of rainwater)
  - Solvent (recycling)
  - The whole process, from raw material to final product, through the choice of facilities and cleaning agents.

4.3. Success stories

4.3.1. Optimization of existing processes

Process optimization might be the first step to be performed in order to save energy. By definition, optimization is "*the act of obtaining the best result possible or the effort for achieving the optimal solution under a given set of circumstances. In design, development, processing operation, and maintenance of engineering systems, common goals are either to minimize the cost or maximize the desired profits as product quality and operation yield*" [57]. Thus, in this demarche, energy consumption must be decrease as far as possible since it is related to high costs. In scientific studies, optimization of process is performed regarding only one kind of parameter which is the quality of final extract (yield and selectivity). Operating parameters (temperature, duration, pressure, pH…)

are thus selected to maximize this criterion, despite they might be related to high energy consumption. Therefore, with the increasing interest in energy saving, more and more processes or equipment are designed considering this aspect. An important tool for the development of energy efficient processes are validated physico-chemical process models, which allow for the simultaneous assessment of process performance and robustness as well as energy efficiency and cost effectiveness. Examples of these process models and their benefit has been demonstrated for different processes and unit operations:

- Pressurized hot water extraction of 10-deacetylbaccatin III from yew for industrial application [39]
- Quality-by-Design (QbD) process evaluation for phytopharmaceuticals on the example of 10-deacetylbaccatin III from yew [58]
- Systematic and Model-Assisted Evaluation of Solvent Based- or Pressurized Hot Water Extraction for the Extraction of Artemisinin from Artemisia annua L. [40]
- Systematic and Model-Assisted Process Design for the Extraction and Purification of Artemisinin from Artemisia annua L.—Part I: Conceptual Process Design and Cost Estimation [59]
- Systematic and Model-Assisted Process Design for the Extraction and Purification of Artemisinin from Artemisia annua L.—Part II: Model-Based Design of Agitated and Packed Columns for Multistage Extraction and Scrubbing [60]
- Systematic and Model-Assisted Process Design for the Extraction and Purification of Artemisinin from Artemisia annua L.—Part III: Chromatographic Purification [61]
- Huter: Systematic and Model-Assisted Process Design for the Extraction and Purification of Artemisinin from Artemisia annua L.—Part IV: Crystallization [62]

Another example is the optimization of mechanical oil extraction from *Jatropha curcas* L. seeds, published by Karaj and Müller [63]. In this study, the objective was to optimize the process increasing oil recovery efficiency and decreasing oil residues in remaining press cake. Various variables were investigated, including specific energy input applied to the mechanical cylinder screw press used for extraction. The first results showed that the higher oil recovery was obtained with a seed material throughput of 4.00 kg/h (around 90 %), however specific energy input related was too high compared to other throughputs. A correlation of specific energy input and oil recovery efficiency versus material throughput was demonstrated, and it enabled to determine the optimal material throughput to maximize both oil recovery and energy efficiency.

4.3.2. Energy recovery

Energy recovery during any process is a new challenge for industrials. Indeed, a process uses only a part (more or less important) of provided heat (called useful heat) [64]. The remaining part is said to be “fatal”, and if it is not recovered and recycled. In extraction field, most processes are performed at solvent boiling point and therefore need an external heat source. Basile *et al.* published a work at laboratory scale about extraction of flavor compounds from rosemary by superheated water [65]. This process was compared with conventional steam distillation in terms of extraction efficiency and energy and water costs. Water is one of the solvents which need the highest energy to be heated and converted at gaseous state. This study claimed that much more heat could be recycled in a superheated water extraction, depending, however, on heat exchangers size. Heat advantage of superheated water extraction per kg of water is announced to be about 20 compared to steam distillation, which makes it viable for up-scaling purpose. Therefore, when designing a new process or optimizing an existing one, energy advantage related and potential to recover heat must be taken into consideration as far as possible.

4.3.3. Process intensification and innovation

When conventional extraction processes are not enough efficient to recover acceptable yields of specific compounds of interest from raw material, it is possible to intensify and assist the process with innovative technologies. Ultrasound (US) or Microwave (MW) can be used for this purpose. They have been hugely employed to intensify extraction of various compounds from various plant materials.

Generally, it results in the decrease of extraction duration and energy consumption compared to conventional process, for similar or enhanced extraction yields. In the case of rosemary, the application of US or MW to extraction media enabled to increase by three times the yield of total phenols extracted compared to corresponding conventional extraction [66]. US technology was also employed by Paniwnyk *et al*. to intensify antioxidants extraction from rosemary, and it resulted once again in improved extraction yields [67].

When optimization of existing process or addition of external technologies during the process are not viable energetically, it is sometimes necessary to reconsider completely global procedure. Innovative process may be adopted for pre-treatment phase upstream from extraction process, or may be the process itself. The main innovative technologies which can be used in current extraction field at industrial level are summarized figure 3.

In much cases, these innovative technologies appear as energy efficient since they enable to reach maximal yields in reduced extraction time. Performed upstream from the main process, they permit an optimal pre-treatment of raw material. For example, US pre-treatment was performed for 30 min prior to HD of *Carum carvi* L. seeds. It resulted in rapid release of EO during HD, that is 80 % of EO recovery in 30 min against 90 min without pre-treatment [68]. In another case, deodorization by instant controlled pressure drop (DIC) was performed on rosemary leaves before ethanolic extraction. It permitted to improve significantly rosmarinic acid (RA) extraction yield since that of DIC-treated leaves was twice as much as untreated leaves. Moreover, DIC-treatment step enabled to recover EO and consequently deodorize plant material. EO extraction was also intensified as DIC-treatment lasted 3 min against minimum 4 h for conventional HD [69]. As last example of successful plant material pre-treatment with innovative process, Kubra *et al*. compared different drying method to dehydrate ginger. MW drying resulted in reduced drying time and maximal volatiles retain in specific conditions [70].

Innovative technologies also offer efficiency opportunities as main extraction process. Pressurized liquid extraction (PLE) appears particularly as an efficient and sustainable approach in various studies. Indeed, Hu *et al*. used this process to extract phenolics from ginger with ethanol or water as solvent [71]. It resulted in reduced extraction time and solvent consumption, and consequently in a decrease of energy consumption and costs.

5. Principle 4: Production of co-products instead of waste towards bio-refinery concepts

5.1. Context

A remarkable growth of circular economy will rely on new technologies moving towards sustainable processes. Instead of applying linear production patterns, resources are used, recovered and renewed which creates further added value of the process [72]. Biorefinery is a concept defined according to the International Energy Agency (IEA) as “the sustainable processing of biomass into a spectrum of marketable products” [73]. Biorefinery is an industrial plant, or a network of plants, which transforms the biomass into its constituents and simultaneously produces energy, biofuels, chemicals and materials, that preferably have added value. It has a comprehensive range of various combined technologies [74]. This approach is wide-ranging; it covers all the sustainability aspects including economy, environment and society [75]. It is becoming widely accepted since the worlds natural resources are constantly decreasing. The concept can be applied in many industrial productions, such as extraction of natural products that are further used as ingredients, food supplements and bioactive compounds [76]. Technologies such as microwave, ultrasound, subcritical and supercritical fluid extraction along with other enabling technologies can provide the efficient extraction with low solvent and energy consumption in the biorefinery system [77, 78]. Three relevant examples of this approach are the full valorisation of co-products and by-products from the production chain wine, orange juice and olive oil.

5.2. Good practices guidelines

Good practices guidelines regarding the management of extraction waste and by-products have two main objectives:

- The development of valorization pathways for a better use of raw material and complete exploitation of by-products
  - Performing a second extraction/process to generate other high value products
  - Using residual raw material to feed livestock
  - Converting the residual biomass into energy
- The reduction of effluents and waste in terms of quantity and harmfulness with:
  - The well-reasoned conception of processes to anticipate and reduce waste production
  - The limitation of liquid and gaseous effluents, particularly greenhouse gases
  - The choice of low environmental impact recycling processes.

5.3. Success stories

5.3.1. Grape

The winery industry generates large amounts of solid waste. Namely, over 30% of grapes used finish as waste (Figure 4). Two main by-products are grape pomaces (10%-20% of processed material) and stems (2%–8%). These by-products are not considered as hazardous waste. However, the high organic matter content can contribute to the pollution, due to the high chemical and biological oxygen demand [79]. Traditionally, these materials are used in biogas production or as fertilizers, however a higher economic income can be expected from the isolation of value-added constituents. The recovery of by-products and co-products is the key point for the “zero waste” winery industry development [80].

Grape pomace is composed of approximately 50% skins, 25% stems and 25% seeds. The main compounds present are 30% neutral polysaccharides, 20% acid pectic substances, 15% insoluble proanthocyanidins (tannins), lignin, proteins, phenols and essential fatty acids from grape seeds [80, 81]. Due to the aforementioned composition, grape pomace is a material that can be utilized in different processes, namely, in the polyphenols (anthocyanins, flavonols, flavanols, phenolic acids, and resveratrol) and grape seed oil extraction, as well as in citric acid, methanol, ethanol, and xanthan production by fermentation [82]. Martinez et al. [81] proposed a cascading biorefinery platform for the valorization of grape pomace aiming to obtain polyphenols, volatile fatty acids, polyhydroxyalkanoates and biomethane. First, the polyphenols were extracted using supercritical CO_2 extraction (SCE) containing ethanol as co-solvent and compared with a conventional methanol extraction. SCE allowed the recovery of 90% of the total polyphenols extracted by conventional method. Volatile fatty acids were produced by anaerobic acidogenic digestion and were used afterwards for the biotechnological polyhydroxyalkanoates production. Furthermore, the solid remains of anaerobic acidogenic digestion were used for CH_4-rich biogas production. A successful example of grape pomace biorefinery was recently demonstrated [82].

5.3.2. Orange

Oranges, in tropical and subtropical regions around the world, represent by far the most cultivated class of commercial citrus fruits. Orange fruit processing results in a large yield of by-products (around 50% of the fruit), which is composed mainly of peels, pulp, and seeds (Figure 4) [83]. It is estimated that the amount of orange peel waste (OPW) generated annually from fresh juice production is over 1 million tonnes [77]. The OPW is typically dried to obtain the peel pellets which are sold as cattle feed at a low price [84]. Nevertheless, OPW consists of many value added compounds that can be recovered, namely: essential oils (D-limonene), pectin, dietary fibres, proteins, enzymes, citric acid, flavonoids, sugars an ascorbic acid [77, 85]. Fidalgo et al. [86] performed an extraction of essential oils and pectin from orange and lemon peels via microwave hydrodistillation (solvent-free microwave extraction) and by microwave extraction combining hydrodiffusion and gravity [86]. Essential oils act as antibacterial, antimycotic, antiviral, and antiprotozoal agents, and pectin is used in various food products as it acts as a hydrocolloid [85, 87]. In this study, high yield of this co-products was obtained. Citrus pectin obtained was characterized by DRIFT spectroscopy and it showed exceptional properties, such as elastic structure and higher setting temperature [86].

Boukroufa et al. [83] presented an orange peel biorefinery using ultrasound- and microwave-assisted extraction to obtain essential oil, polyphenols and pectin. A solvent-free process exploiting the ‘‘in situ’’ water which was recycled and used as solvent. The essential oil extraction was performed by microwave hydrodiffusion and gravity (MHG) and compared to conventional steam distillation extraction. There was no significant difference in the essential oil yield and composition comparing these two methods. Later on, residual water of plant obtained after MHG extraction was used as a solvent for polyphenols and pectin extraction from MHG solid residues. Polyphenols were extracted by ultrasound-assisted extraction (UAE) and conventional method. UAE was much more efficient in polyphenols extraction. Pectin was recovered using conventional and microwave-assisted extraction (MAE). MAE provided a higher pectin yield and a drastic decrease in extraction time. The recommended platform allows the recovery of various co-products in short time using only a natural by-product as a matrix [83].

5.3.3. Olives

Extra-virgin olive oil (EVOO) is in the centre of the Mediterranean diet pyramid, and its beneficial health effects have been recently recognised by the American FDA [88]. In the last decades the EVOO production has been steadily increased [89]. Olive oil production generates a large amount of by-products, namely olive tree pruning biomass (OTPB), olive leaves, olive stones, pomace, and olive mill wastewaters (OMWW), which refers to all wastewater streams generated in the oil production [90]. The high polyphenolic content in production wastes showed a high phytotoxicity and their disposal generates environmental concerns. Meantime these by-products could be a source of valuable compounds [89]. In the EU-28, olive oil industry generates annually 9.6 million tonnes of by-products that could be valorised as well as 11.8 million tonnes of OTPB only in part valorised (30%). Therefore, olive oil production in the EU-28 generates annually 13.1 million tonnes of by-products for different applications. Olive leaves are a mixture of leaves and small branches that are generated both during the olive trees pruning, as well as during the harvesting and cleaning of olive fruit before the oil extraction [91]. In the olive leaves structure different bioactive compounds, that possess therapeutic and functional effect, are present. Therefore, olive leaves extraction has been extensively studied both in the lab- and industrial-scale [90]. Phenols that can be found in olive leaves are various: flavones (luteolin-7- glucoside, apigenin-7-glucoside, diosmetin-7-glucoside, luteolin, and diosmetin), flavonols (rutin), flavan-3-ols (catechin), substituted phenols (tyrosol, hydroxytyrosol, vanillin, vanillic acid, and caffeic acid) and secoiridoids (oleuropein). The most prevalent phenol is oleuropein, which is intensively studied for its promising effects on human health and its medical potential [92]. It contributes to the lowering of blood pressure and blood glucose levels in diabetic individuals and improves the metabolism of lipids [93]. It is also a strong antioxidant, and possesses anti-inflamatory, anti-cancer, anti-viral and many other health promoting effects [94]. Sahin et al. [95] optimized the extraction of total phenolic content (TPC) and oleuropein from olive leaves in solvent free microwave assisted extraction. In only 2 minutes 0.06 ppm of oleuropein and 2.48 ppm of TPC were extracted. Moreover, the extracts showed antibacterial activity against *Staphylococcus aureus* and *S. epidermidis* [95].

Olive pomace represents, by weight, the main olive oil by-product. It is consisted of crushed olive stones, vegetation water, process water, and all materials coming from the fruit except olive oil [96]. Olive pomace can be generated through two different olive oil extraction procedures, namely two-phase and three-phase system. By applying two-phase system two fractions are obtained in the decanter and the additional centrifugation of olive oil is performed. Whereas performing the three-phase system the water is added in the decanter and three phases are obtained (olive oil, pomace and waste water). Therefore, the main difference between these two separation methods is the higher water content of the olive pomace from the two-phase method (more than 60% vs. less than

50% in the three-phase system). The olive pomace is usually further subjected to the residual oil extraction (2–3% w/w of olive pomace), including the removal of crushed stones [97]. Obtained olive pomace contains many phytochemicals including tocopherols, flavonoids, quercetin, cinnamic acid, peptides and phenolic compounds [92]. Schievano et al. [98] performed an extraction of polyphenols and mono/poly-unsaturated fatty acids using SCE and ethanol as a co-solvent. The freeze dried extract contained valuable unsaturated fatty acids, squalene and several polyphenols, of which the most abundant was di-hydroxytyrosol. The extraction was followed by thermochemical (oxidation or pyrolysis) recovery of energy, biofuels and materials [98].

6. Principle 5: Reduction of unit operations number and development of safe, robust and controlled processes.

6.1. Context

With current economic and environmental concerns, extraction industry must develop efficient processes in terms of extraction yields, cleanliness to environment, safety of operators and use of space. This approach is part of process intensification demarche illustrated in figure 5. More precisely, intensification aims at increasing extraction yield, extract purity and quality, while decreasing extraction time, number of unit operations, energy consumption, environmental impacts, economical costs, quantity of solvent and total waste.

Generally, a whole extraction process is composed of following essential steps:

(1) Plant material pre-treatment: raw material must be previously dried and ground to increase surface contact area and solvent penetration level;
(2) Solid-liquid extraction with appropriated solvent;
(3) Solid-liquid separation by filtration or centrifugation;
(4) Solvent removal and recycling under vacuum to eliminate every trace of residual solvent in final extract.

Such process is often very long, and results in high energy consumption, particularly due to fourth step. To overcome this problem, intensification may be achieved, for example by designing smaller size units and by reducing the number of unit operations. Ideally, it may result in a better use of process inputs (raw material, energy…), a superior control of global process and a reduced global environmental footprint.

6.2. Good practices guidelines

Beyond energy efficiency described (Principle 3), a process must present other essential characteristics to meet the definition of green extraction process such as :

- Intensification of global process using innovative technologies
- Reduction of the number of unit operations by deep study of the process
- Development of more compact unit operations
- Ensure the global safety and robustness of the process
- Total control of the process and flux related

6.3. Success stories

6.3.1. Reduction of unit operations

In a whole extraction process, solvent elimination from both extract and spent plant residue after extraction is one of the limited stage. It is even time and energy consuming if boiling point of solvent is high. Moreover, it may cause the degradation of sensitive compounds in final extract, particularly when too hard experimental conditions are applied. Therefore, the question of solvent removal is a real concern in current extraction field: it may result in a loss of final extract quality, but it is nevertheless a necessary step, particularly when extraction is performed with organic solvents. However, in certain cases, some alternative solutions can be adopted to skip this step, particularly:

- Using solvent which can be removed directly after extraction process without concentration step;
- Using solvent that forms part of final extract formulation.

Plant extraction with supercritical CO_2 as solvent is a perfect example to illustrate the first solution. CO_2 is gaseous at atmospheric pressure. Therefore, after extraction under supercritical conditions (T_c=31 °C; P_c=73.8 bar), pressure is brought back to atmospheric level, and it results in direct removal of gaseous CO_2 from the extract [99]. Instantaneously, final extract is safe, exempt from any residual solvent and ready for further purification or formulation steps. As an example, valuable products extraction from rosemary and ginger using supercritical CO_2 is hugely reported in current literature, particularly the recovery of EO, oleoresin or low polarity antioxidants [100].

In other cases, it is possible to perform plant extraction directly in final formulation solvent. Actually, compounds of interest are extracted from plant material and immediately solubilized in final formulation solvent. This approach enables to skip not only solvent removal step after extraction, but also that of formulation. First of all, the example of aromatized oils can be cited. In most cases, vegetable oils are aromatized with EO previously extracted with organic solvents or by HD. However, in 2010, Veillet *et al.* proposed an original procedure for direct aromatisation of olive oil with basil [101]. Basil leaves were directly immersed in olive oil and US were applied to the mixture in order to accelerate diffusion of basil volatile into the oil. Their use enabled to reduce extraction time from hours or days with conventional maceration (CM) to 20 min. Aromatization using this procedure accounts only one unit operation against several using conventional way. The same approach was adopted by Li *et al*. in 2012 to produce vegetable oil enriched with carotenoids [102]. As illustrated in figure 6, number of unit operations was drastically reduced compared to conventional procedure, particularly with the elimination of carotenoids extraction with organic solvent and solvent removal steps.

6.3.2. Automatized and compacted equipment

Conventionally, characterization of plant raw material is performed using a Soxhlet extractor. This method is time-consuming (extraction lasts at least 8 h), and consequently requires a lot of energy [103]. Moreover, extractions must be performed one after another, and the elimination of solvent in next step requires long concentration time, particularly when large volumes are involved. In order to intensify the process, Ankom Technology proposes an automated Soxhlet extractor (Ankom^{XT15} extractor) to determine crude fat and oil content. This equipment is fully automatized and consequently handlings errors are avoided. Initial raw materials are encapsulated in specific filters which are afterwards placed in the reactor (until 15 samples at a time). The process is accelerated by performing the extraction under pressure at elevated temperatures. This extractor enables to perform 15 extractions at a time and a total daily volume of more than 150 samples. After extraction, crude fat and oil content is determined by weight difference of plant material before/after extraction. Regarding extraction solvent, recovery and recycling is done automatically at a rate of around 97 %.

This kind of equipment is efficient, compacted, sure, well-controlled and enables to save time, money and place, and therefore in accordance with principle 5 specifications. The main disadvantage is that final extracts are not recovered at the end of the process, which avoid potential determination of extract composition.

As another example, VELP® society developed an automatic solvent extractor (SER 158) to extract a wide range of plant materials. First of all, sample is placed in extraction thimble and immersed in boiling solvent for an effective extraction of active compounds. The choice of solvent and extraction duration is realized by user. After extraction, solvent level is decreased below extraction thimble. A part of solvent is collected in recovery tank and the other part continues to flow through the sample to complete previous extraction step. Then, solvent is completely collected in recovery tank. Finally, heaters are switched off and glassware is lifted to prevent burning of dried extract.

This equipment proves a perfect match with principle 5 requirements. Indeed, it is extremely compact as six extractions can be performed at a time in a reduced space. Moreover, it enables to obtain reliable results with excellent reproducibility. Solvent recovery is about 90 % and water consumption is limited, which permit to save energy and cost. Finally, last but not least, the process is operator-friendly since it is easy to use and safe with user exposure to solvent is minimized.

7. Principle 6: Aim for green extract with green values and non-denatured and biodegradable extract without contaminants.

7.1. Context

The concept of naturalness is quite difficult to define, particularly in the case of plant extract where the definition of genuine natural extract is unclear.

According to REACH legislation [104], a natural substance is "a naturally occurring substance as such, unprocessed or processed only by manual, mechanical or gravitational processes, by dissolution in water, by flotation, by extraction with water, or by steam distillation.

This definition includes that the substance must not be chemically modified, in other words its molecular structure must remain unchanged independently of the process performed, even if it is chemical. Thus, according to this legislation, olive oil or fruit and vegetable juices for example can be considered as "natural". However, this definition does not bring any details about solvent extraction process, excepted that it can be performed with water to ensure the naturalness of final extract. Thus, the naturalness of extracts obtained with such process is controversial and different point of view are represented. In some cases, solvent extraction is considered as a physical process, and the generated extract is considered as "natural", provided the solvent is removed at the end of the process. In other cases, the naturalness of the final extract is controlled by the type of solvent used for extraction. The latter must be natural or of natural origin to ensure naturalness. Still others refute the naturalness of extracts when they are obtained by extraction with a solvent other than water [105-106]. Therefore, naturalness of the extract obtained by extraction using a solvent is subject to debate. Finally, last but not least, the global naturalness of an extract also depends on the nature of initial plant material, which must be provided by well-reasoned sourcing as far as possible.

In this context, the ISO 16128 standard provides guidelines for technical definitions and criteria for natural and organic cosmetic ingredients and products. In addition, we can notice that naturalness is very often associated to "organic" aspects. For example, Ecocert and Cosmos certifications are essential in cosmetics sector and deal with both aspects. They are associated to detailed guides governing the chemicals and solvents authorized as well as the processes and facilities adapted to produce certified organic and natural extracts or product [107,108].

Various other appellations or labels referring to naturalness can be found on extracts or final products packaging in the different sectors activities (Figure 7). Each of them is associated to a specific charter of good practices, relating to the type of raw material, chemicals, processes and additives authorized. All of these labels aim principally at sending a particular message to the consumer which feels more secure and reassured about what he buys.

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7.2. Good practices guidelines

To be considered an "eco-extract", it must have most of the following characteristics (Figure 8): natural, high quality with active and undenatured compounds, high functionality (antioxidant, antimicrobial, flavor, coloring properties. ..), in accordance with specific legislation concerning the sector of application (agri-food, cosmetics, pharmaceutical industry ...), with a low environmental footprint (determination with the LCA approach).

7.3. Success stories : Towards new definitions of Green Extract(s)

7.3.1. Deoxyribo Nucleic Acid (DNA)

One way of providing a response to the naturalness would be to determine the DNA of the extracts obtained. The enterprise DNA Gensee proposes, thanks to advances in molecular biology and advent of next-generation DNA sequencing techniques, an opportunity to know exactly which plants are present in cosmetic product, food supplement or drug-based of plants. From DNA traces, DNA Gensee proposes to detect and identify the plant species used in the composition of the analyzed substrates which could be a proof of naturalness. The concept can go further in order to design new processes that do not denature DNA, thus not denaturing the "Naturalness" of the product.

7.3.2. Quality

The quality of the extract is generally determined considering the content of active compounds and the absence of denatured molecules. During an extraction process, degradation of compounds of interest may occur depending on process conditions, such as high temperature, presence of oxygen or long extraction time. This phenomenon of degradation must be avoided as far as possible since degradation products can affect the organoleptic and the nutritive properties of final extract. For example, ultrasound assisted extraction (UAE) of raw material containing lipids may result in the formation of radicals and consequently off-flavors in the extract.

In the case of dyes, unsuitable extraction conditions (high temperature, light, or presence of oxygen) may increase the kinetics of beta-carotene oxidation. In addition, degradation compounds may represent a threat for final consumer which is in direct contact with the product (ingestion or skin absorption). Since the emergence of green chemistry, innovative processes are increasingly used and allow an intensification of the process by working at lower temperature, without solvent and with the least unit operations.

7.3.3. Functionality

By definition, functionality is "the quality of having a practical use". Natural extracts are considered as functional when they aim at accomplishing a particular task in the final foodstuffs or cosmetics in which they are added (coloring, antioxidant, texturing ...). Hence, the formulation step is essential to ensure the best performance of the resulting extract. For example, the polarity of the extract must be compatible with the polarity of final product.

Measuring of extract functionality is quite difficult to implement routinely at industrial level, that's why natural extracts are generally standardized according to their content in active compounds. However, it must be kept in mind that composition and functionality do not always point to the same direction. Moreover, when activity and functionality are assessed, it should be recognized that results are influenced by the nature of the tests carried out, depending on whether they take place in polar systems where polar compounds are favored over less polar molecules to react since they are more soluble, hence more available for reaction.

7.3.4. Safety

Safety is a crucial criterion in "eco-extract" definition. First of all, the extract must be exempt from any microbial contamination. For this purpose, extracts can be pasteurized or submitted to sterilizing filtration at the end of the process. Besides microorganisms, the most common contaminants found in natural extracts include pesticides, polycyclic aromatic hydrocarbons (PAH) and heavy metals. Most of the cases, they are transferred from contaminated soils to plant material during agricultural production. After plant extraction, according to the solvent used, such compounds are found in very high quantity in the final extract and very often beyond any quantitative limits. Actually, extraction process tends to concentrate the contaminants initially present in raw material in the final extract since these molecules are also soluble in the solvent and extracted at the same time as active compounds. To limit or avoid this phenomenon, plant material sourcing must be well reasoned as far as possible, for example using raw material proceeding from organic farming [109]. Another solution is a previous step of plant material decontamination before extraction [110] or sometimes even during the extraction using absorbent materials [111].

7.3.5. Legislation

The development of "eco-extracts" cannot be performed without considering legislation aspects. Regarding the sector to which they are dedicated, extracts must be in accordance with specific legislations related. Indeed, a very large number of legal documents, regulations or directives governs the foodstuffs, cosmetics or pharmaceuticals products, whether regarding their composition, their safety or their labeling. For example, in food processing sector, the use of additives including some natural extracts are governed by various regulations such as n° 1333/2008. More specific regulations exist for specific cases as Regulation (n° 1334/2008) dedicated to flavoring ingredients. The use of solvents for the production of foodstuffs and food ingredients is also regulated, particularly by Directive 2009/32 / EC, which establishes maximal solvent residue limits in the final foodstuffs.

Among the foodstuffs and food ingredients, including some natural extracts, we can also find the category of "novel food". By definition, novel foods are foodstuffs or ingredients which were not consumed in European Community before 1997. They are governed by Regulation n° 258/97 of 27 January 1997. According to the legislation, novel foods include:

- Foods and food ingredients produced from genetically modified organisms (GMO), but which does not contain such compounds;
- Foods and food ingredients with a new or intentionally modified primary molecular structure;
- Foods and food ingredients consisting of or isolated from micro-organisms, fungi or algae;
- Foods and food ingredients consisting of or isolated from plants and food ingredients isolated from animals, except for foods and food ingredients obtained by traditional propagating or breeding practices and having a history of safe food use;
- Foods and food ingredients from a manufacturing process not currently used. This process gives rise to significant changes in the composition or structure of the foods or food ingredients which affect their nutritional value, metabolism or level of undesirable substances.

As examples, phytosterols or extract of magnolia bark are included in this category of food ingredients

Before being authorized for commercialization, the potential toxicity of these ingredients and the eventual nutritional imbalance induced by their introduction in the global diet have to be assessed by relevant institutions. Final decision rests with the European Commission which, after consulting the European Food Safety Authority (EFSA), accepts or not the new ingredient as a novel food.

7.3.6. Life cycle analysis

As last but not least requirement, a “green extract” or an “eco-extract” must have a low environmental footprint. This parameter can be determined using a life cycle analysis (LCA) approach born in a context of sustainability. It is a multi-criteria study aiming at quantifying the potential impacts of a product or service during its whole life cycle, from the cradle to the grave [112]. Impacts (positive or negative) can be environmental, economic or social. The Whole life cycle of a product considers all the stages of the life of the product. It includes the extraction of raw materials, the processing, the distribution and transport, the utilization, maintenance and finally the end-of-life treatment. Each stage is analyzed according to the flows of materials and energies that it needs.

The methodology to perform an LCA is described in norms ISO14040 to ISO14044. Actually, it is a multi-step approach. The first step is the definition of the functional unit. It is a key component for the study. It must be determined carefully and the same functional unit must be kept if one aims at comparing different life cycles. If not, that doesn’t make any sense: indeed, a process can have less negative impacts on environment but perhaps the final extract recovered is less performant or is a low-quality extract compared to those from the more polluting process.

Secondly, a Life Cycle Inventory (LCI) has to be done. It consists in an assessment of inputs and outputs for each step of the life cycle and they must be reported to the functional unit. Inputs are energy and non-energy resources, and outputs are emissions into water, soil and air, waste and by-products. A complete LCI from the cradle to the grave is often quite difficult and heavy to perform. Data are not always available. A gate to gate approach more focused on the process is sometimes adopted (figure 9) to facilitate the study. At industrial level, data can be collected directly in the production sites. This approach is useful particularly to compare processes in terms of environmental efficiency. However, in the case of natural extracts, it is recommended to consider also the agricultural step (plant growth and harvest before it use for extraction) and the recycling and treatment of extraction by-products.

The next step after LCI is the transformation of data into impacts. For this purpose, there are various LCA software available with implemented databases. Some of them are dedicated to specific sectors of activity. We can cite for example Food’Print v-1 for agri-business or BEE V3.1 for packaging. Open LCA and SimaPro are examples of more universal software which can be used in extraction field. Databases such as Ecoinvent 2.1, Agribalyse, ELCD or LCA Food can be implemented by default, but it is generally possible to add the database of its choice in the program used.

Therefore, LCA software enables to convert data from LCI into impacts. Actually, depending on the program used, different types of impact can be chosen. The most common are greenhouse effect, euthrophisation, acidification, ozone depleting, eco-toxicity and fossil resources depletion. They correspond to "midpoint" impacts dedicated to scientific or advertised community. It is also possible to express the results into damages, particularly for communicating with non-advertised public. In this case, we can talk about human health, increase of cancer rate or loss of biodiversity for instance.

The mode of action of the software is very simple. The life cycle of the product is firstly separated into its different constitution blocks, in a more or less detailed way. For example, the block corresponding to the fabrication can be divided into the different operation units. Then, the contribution of each step regarding each impact is calculated using algorithms. Results can be expressed in a table or as a graphic. Besides determining the global environmental footprint of a product, it enables to see which step in the life cycle is more impacting for potential improvement.

The use of an LCA approach makes it possible to compare situations and to identify the movements of pollution from one natural environment to another, or from one stage of the life cycle to another. This knowledge of the different impacts of products allows companies to prioritize improvements and inform technical choices.

Life cycle analysis is therefore a decision support tool. The results obtained can in fact be used for eco-design, environmental labeling or to enable companies to choose an industrial policy: choice of product design and improvement, choice of process, etc. The strength of an LCA lies in the quality of the databases used, which is currently a limiting step to the realization of these databases.

8. Future directions and challenges.

Plant based extracts/products have been used probably since the discovery of fire. Egyptians and Phoenicians, Jews and Arabs, Indians and Chinese, Greeks and Romans and even Mayas and Aztecs all possessed a culture of using plants as source of reagents for cosmetic, perfumery, medicine, food ingredients and products, colors and dyes, and building materials. Until the start of the petroleum era plant-derived biomass was the main source of reagents, ingredients and products for food and non-food applications. The spectacular growth of petroleum-based processes led to a withdrawal from those based on biomass. However, the depletion of fossil resources, upon which the current European and International industry and economy heavily depends, and environmental considerations force us towards a post-petroleum society. The challenges launched by the environment protection and competitiveness of the globalized world strongly require innovations that break away from the past rather than simple continuity.

Plant-based extraction could be one of the solutions from the past to the future of humanity as an ecologic and an economic chemistry, and as a success story of Green Chemistry in the 21th century. Nowadays, based on research and innovations in the 20th century, we can in one side make cultivation and harvest in respect biodiversity a huge number of biomass (plant, macro and micro algae, fungi, yeast…), and in the other side we have mature refineries which could transform petrol as a mixture liquid form to variety of reagents and products. If we want to have a bio-refinery based on plant products, there is a missing link between cultivated and harvested products and bio-petrol as a complex mixture extracted from these biomass in liquid form to be refined in multiple reagents, synthons, ingredients and products for variety of applications. This important bridge is based on extraction processes which could extract separate primary (lipids, proteins, carbohydrates) and secondary metabolites (terpenes, polyphenols, alkaloids…) from the solid plant matrix.

Extraction as a unit operation and technique appear to be a simple and mature chemical or chemical engineering process. However, it is more complicated than it seems. Existing conventional processes have some major drawbacks, such as insufficient recovery of extracts, extensive extraction duration, intensive heating and/or mixing, resulting in high energy consumption. Moreover, due to toxicity and the growing price of fossil resources, replacement of solvent of petroleum origin is desirable. In a bio-refinery concept dealing with extraction of natural products, "innovative" extraction processes should focus on intensification: faster and more effective energy use, increased mass and heat transfer, reduced equipment size, elimination of petroleum solvents, and reduction of processing steps. In another side, extract must meet a number of quality criteria, contrary to some popular misconceptions; the "natural" state of the extract is no guarantee of its harmlessness to man and the environment.

In such changing context, nowadays we must include the change of extraction conscience from a simple interest in data analysis to interest in models and the strong consideration of the environmental side effects of our practice as a consequence of the high demand of extraction information. Green extraction of naturals products could be a new concept to meet the challenges of the 21st century, to protect both the environment and consumers and in the meantime, enhance competition of industries to more ecologic, economic and innovative. Within the green and innovative extraction approach, the green extract obtained in such way to have the lowed possible impact on the environment (less energy and solvent consumption etc,) and whose eventual recycling would have been planned for (co-products, biodegradability etc). This green extract should be the result of a whole chain of values in both senses of the term: economic and responsible, starting from the production and harvesting of the plant, the transformation process of extraction and separation together with formulation marketing.

REFERENCES

[1] P.T. Anastas, J.C. Warner, Green chemistry: Theory and practice, Oxford University Press, London, **1998**. ISBN: 9780198506980

[2] P.T. Anastas, J.B. Zimmerman, Desing through the twelve principles of green engineering, Environment Science and Technology 37 (**2003**) 94-101. **DOI:** 10.1021/es032373g

[3] F. Chemat, M.A. Vian, G. Cravotto, Green Extraction of Natural Products: Concept and Principles, International Journal Molecular Science 13 (**2012**) 8615–8627. doi: 10.3390/ijms13078615.

[4] F. Chemat, J. Strube , Green Extraction of Natural Products. Theory and practice. Wiley-VCH, Weinheim, **2015**.

[5] E. Ibanez, A. Cifuentes, Green Extraction Techniques: Principles, Advances and Applications, Elsevier, Amsterdam, **2017**. **ISBN:** 9780444638694

[6] J. Azmir, I.S.M. Zaidul, M.M. Rahman, K.M. Sharif, A. Mohamed, F. Sahena, M.H.A. Jahurul, K. Ghafoor, N.A.N. Norulaini, A.K.M. Omar, Techniques for extraction of bioactive compounds from plant materials: A review, Journal of Food Engineering 117 (**2013**) 426–436. https://doi.org/10.1016/j.jfoodeng.2013.01.014

[7] B. Kaufmann, P. Christen, Recent extraction techniques for natural products: microwave-assisted extraction and pressurised solvent extraction, Phytochemical Analysis, 13 (**2002**) 105–113. DOI:10.1002/pca.631

[8] M. Colin, D. Guenard, F. Gueritte-Voegelein, P. Potier, Dérivés du taxol, leur préparation et les compositions pharmaceutiques qui les contiennent. EP 0253738 A1, 16 juil. 1987.

[9] J Prohens, F. Nuez Handbook of plant breeding: Vegetables I, Springer, New York, NY, USA.,2008.

[10] J. Diamanti, M. Battino, B. Mezzetti, Breeding for fruit nutritional and nutraceutical quality. In: Jenks, M.A. and Bebeli, P.J. (eds.), Breeding for fruit quality. John Wiley & Sons Inc., Hoboken, NJ, USA, pp. 61-80, **2011**.

[11] N. Delabays, X. Simonnet, M. Gaudin, The genetics of Artemisinin content in Artemisia annua L. And the breeding of high yielding cultivars. *Current Medicinal Chemistry* 8, (**2001)**, 1795–1801.

[12] M. Azizi, A. Ghani, T. Ebadi, S. Crockett, The Ex Situ Comparison of Two Improved St. John's wort (Hypericum perforatum) Cultivars with an Iranian Wild Population. Acta Hortic., 925, (**2011**), 163–170. DOI: 10.17660/ActaHortic.2011.925.24

[13] R. Komakech, Y. Kang, J. Lee, F. Omujal, A Review of the Potential of Phytochemicals from Prunus africana (Hook f.) Kalkman Stem Bark for Chemoprevention and Chemotherapy of Prostate Cancer. Evidence-Based Complementary and Alternative Medicine 2017, Article 3014019, 10 p. https://doi.org/10.1155/2017/3014019

[14] X. Simonnet, B. Hell, C. Franz, Domestication du podophylle indien (Podophyllum hexandrum Royle): étude sur la germination, Revue suisse Vitic. Arboric. Hortic., Vol. 40 (3) (2008): 179-184.

[15] E. Gontier, A. Clement, F. Bourgaud, A. Guckert, Method for producing metabolites from plants cultivated in soil-less medium. WO0133942 (A1). 17 mai 2001.

[16] M. Cvjetko Bubalo, S. Vidović, I. Radojčić Redovniković, S. Jokić, Green Solvents for Green Technologies. J Chem Tech. Biotech 90(9) (2015) 1634-1639. **https://doi.org/10.1002/jctb.4668**

[17] M. Abert Vian, T. Allaf, E. Vorobiev, F. Chemat, Solvent-Free Extraction:Myth or Reality? in *Alternative Solvents for Natural Products Extraction* (editors: Chemat, F., Vian M.A.) DOI 10.1007/978-3-662-43628-8, (2014).

[18] M. Cvjetko Bubalo, S. Vidović, I. Radojčić Redovniković, S. Jokić, New perspective in extraction of plant biologically active compounds by green solvents. Food en Bioprod Process, 109, (2018) 52-73. https://doi.org/10.1016/j.fbp.2018.03.001, (2018).

[19] F. Chemat, A.S. Fabiano-Tixier, M. Abert Vian, T. Allaf, E. Vorobiev, Solvent-free extraction of food and natural products. TrAC Trends in Analytical Chemistry, 71, (2015) 157-168 . . http://dx.doi.org/10.1016/j.trac.2015.02.021. (2015).

[20] F. Chemat, M. Vian, F. Visinoni, Microwave hydrodiffusion for isolation of natural products. European Patent, EP 1 955 749 A1. (2008).

[21] Y.,Li, , A.S.,Fabiano-Tixier, F. Chemat, Essential Oils as Reagents in Green Chemistry. Springer Cham Heidelberg New York Dordrecht London. DOI 10.1007/978-3-319-08449-7, (2014)

[22] N. Flórez, E. Conde, H. Domínguez, Microwave assisted water extraction of plant compounds. Journal of chemical technology and biotechnology, *90*, (2014). 590-607 DOI 10.1002/jctb.4519, (2014).

[23] M. Plaza, C. Turner, Pressurized hot water extraction of bioactives. TrAC Trends in Analytical Chemistry, 71 (2015), 39-54. http://dx.doi.org/10.1016/j.trac.2015.02.022.

[24] A. Haghighi Asl, M. Khajenoori, Subcritical Water Extraction. In book: Mass Transfer - Advances in Sustainable Energy and Environment Oriented Numerical Modelin, (2013) Chapter: 17, pp.29. http://dx.doi.org/10.5772/54993.

[25] M. Herrero, M. Castro-Puyana, J.A. Mendiola, E. Ibanez, Compressed fluids for the extraction of bioactive compounds. TrAC Trends in Analytical Chemistry, 43, (2013), 67-83. . http://dx.doi.org/10.1016/j.trac.2012.12.008

[26] D. Pingret, A.S. Fabiano-Tixier, C. Le Bourvellec, C. Renard, F. Chemat, Lab and pilot-scale ultrasound-assisted water extraction of polyphenols from apple pomace. Journal of Food Engineering, 111 (2012) 73-81. doi:10.1016/j.jfoodeng.2012.01.026.

[27] S. Tunchaiyaphum, M.N. Eshtiaghi, M. Yoswathana, Extraction of Bioactive Compounds from Mango Peels Using Green Technology. Int. J Chem. Eng. Applicat., 4, (2013) 194-198. DOI: 10.7763/IJCEA.2013.V4.293

[28] A. Naffati, J. Vladić, B. Pavlić, R. Radosavljević, A. Gavarić, S. Vidović, Recycling of filter tea industry by-products: application of subcritical water extraction fornrecovery of bioactive compounds from A. uva-ursi herbal dust. J. Supercrit. Fluids, 121, (2017) 1- 9. https://doi.org/10.1016/j.supflu.2016.11.010

[29] A. Tomšik, B.Pavlic, J. Vladić, M. Cindric, P. Jovanov, M. Sakač, A. Mandic, S. Vidović, Subcritical water extraction of wild garlic (Allium ursinum L.) and process optimization by response surface methodology. J Supercrit. Fluids, 128, (2017) 79-88. DOI: 10.1016/j.supflu.2017.05.012

[30] B. Pedras, M. Salema-Oom, I. Sá-Nogueira, P. Simões, A. Paiva, S. Barreiros, Valorization of white wine grape pomace through application of subcritical water: Analysis of extraction, hydrolysis, and biological activity of the extracts obtained. J. Supercrit. Fluids, 128, (2017) 138-144. https://doi.org/10.1016/j.supflu.2017.05.020

[31] J. Vladic, O. Canli, P. B.avlic, Z. Zekovic, S. Vidovic, M. Kaplan, Optimization of *Satureja montana* subcritical water extraction process and chemical characterization of volatile fraction of extracts. J Supercrit. Fluids, 120, (2017) 86-94. DOI10.1016/j.supflu.2016.10.016

[32] H. Xu, W. Wang, X. Liu, F. Yuan, Y .Gao, Antioxidative phenolics obtained from spent coffee grounds (*Coffea arabica* L.) by subcritical water extraction. Industrial crops and products, Ind. Crops Prod. 76, (2015) 946-954. DOI: 10.1016/j.indcrop.2015.07.054

[33] M.E Yulianto, P.Kusumo, I. Hartati, , Wahyuningsih., Subcritical water extraction of gingerol from *Zingiber officinale*. Rasayan J. Chem., 10, (2017) 738-734. http://dx.doi.org/10.7324/RJC.2017.1031619

[34] C.I. Cheigh, S.Y. Yoo, M.J. Ko, P.S..Chang, M.S.Chung, Extraction characteristics of subcritical water depending on the number of hydroxyl group in flavonols. Food Chem., 168, (2015) 21–26. DOI: 10.1016/j.foodchem.2014.07.047

[35] M.V .Kiamahalleh, G. Najafpour-Darzi, M. Rahimnejad, A.A. Moghadamnia, M.V. Kiamahalleh, High performance curcumin subcritical water extraction from turmeric (*Curcuma longa* L.). J Chrom. B.,1022, (2016). 191-198. **DOI:** 10.1016/j.jchromb.2016.04.021

[36] S.M. Zakaria, S.M. Mustapa Kamal, Subcritical Water Extraction of Bioactive Compounds from Plants and Algae: Applications in Pharmaceutical and Food Ingredients. Food Engineering Reviews 8(1), (2016) 23-34. DOI: 10.1007/s12393-015-9119-x

[37] M. Brahim, F. Gambier, N. Brosse, Optimization of polyphenols extraction from grape residues in water medium, Infustrial Crops and Products, 52, (2014), 18-22. http://dx.doi.org/10.1016/j.indcrop.2013.10.030.

[38] E. Coelho, M.A.M. Rocha, J.A., Saraiva, M.A. Coimbra, Microwave superheated water and dilute alkali extraction of brewers' spent grain arabinoxylans and arabinoxylo-oligosaccharides. Carbohydrate Polymers, 99, (2014), 415- 422. https://doi.org/10.1016/j.carbpol.2013.09.003.

[39] M. Sixt, J. Strube, Pressurized hot water extraction of 10 deacetylbaccatin III from yew for industrial application http://dx.doi.org/10.1016/j.reffit.2017.03.007

[40] A. Schmidt , M. Sixt, M. Johannes Huter, F. Mestmäcker, J. Strube
Systematic and Model-Assisted Process Design for the Extraction and Purification of Artemisinin from Artemisia annua L.—Part II: Model-Based Design of Agitated and Packed Columns for Multistage Extraction and Scrubbing, Process, 6, (**2018**), 179-200 doi:10.3390/pr6100179

[41] M. Khajenoori, A. Haghighi Asl, H. Noori Bidgoli, Subcritical Water Extraction of Essential Oils from *Matricaria Chamomilla* L. International Journal of Engineering **26**(5) (2013), 489-494.
https://doi.org/10.1111/j.1745-4530.2008.00245.x

[42] A. Farhat, A.S. Fabiano-Tixier, M. Maataoui, J.F. Maingonnat, M. Romdhane, F. Chemat, Microwave steam diffusion for extraction of essential oil from orange peel: Kinetic data, extract's global yield and mechanism. Food Chemistry, 127, (2011), 1472-1480 . doi:10.1016/j.foodchem.2010.07.110.

[43] S. Périno-Issartier, C. Ginies, G. Cravotto, F. Chemat, A comparison of essential oils obtained from lavandin via different extraction processes: Ultrasound, microwave, turbohydrodistillation, steam and hydrodistillation. J of Chromatographt A, 1305, (2013), 41-47. . http://dx.doi.org/10.1016/j.chroma.2013.07.024

[44] A. El Asbahani, K. Miladi, W. Badri, M. Sala, E.H. Aït Addi, H. Casabianca, A. El Mousadik, D. Hartmann, A .Jilale, F.N.R. Renaud, A. Elaissari, Essential oils: From extraction to encapsulation. Int J. of Pharmaceutics, 483, (2015), 220-243. http://dx.doi.org/10.1016/j.ijpharm.2014.12.069.

[45] J. Azmir, I.S.M. Zaidul, M.M. Rahman, K.M. Sharif, A. Mohamed, F. Sahena, M.H.A. Jahurul, K. Ghafoor, N.A.N. Norulaini, A.K.M. Omar Techniques for extraction of bioactive compounds from plant materials: A review. J of Food Engineering, 117, (2013), 426-436. . http://dx.doi.org/10.1016/j.jfoodeng.2013.01.014

[46] T.T. Garmusa, L.C. Paviania, C.L. Queirogab, P.M. Magalhãesb, F.A. Cabrala, Extraction of phenolic compounds from pitanga (*Eugenia uniflora* L.) leaves by sequential extraction in fixed bed extractor using supercritical CO_2, ethanol and water as solvents. J. Of Supercritical Fluids, 86, (2014), 4 -14. http://dx.doi.org/10.1016/j.supflu.2013.11.014.

[47] Ž. Knez, E. Markočić, M. Leitgeb, , M. Primožić, M. Knez Hrnčić, M. Škerget, Industrial applications of supercritical fluids: A review. Energy, 77, (2014), 235-243. http://dx.doi.org/10.1016/j.energy.2014.07.044.

[48] J.I. García, H. García-Marín, E .Pires, Glycerol based solvents: synthesis, properties and applications. *Green Chem.* **16**, (2013) 1007 – 1033. DOI 10.1039/C3GC41857J

[49] E. Shehata, S. Grigorakis, S. Loupassaki, D.P. Makris, Extraction optimisation using water/glycerol for the efficient recovery of polyphenolic antioxidants from two *Artemisia* species. Separation and urification Technlology, 149, (2015), 462-469. DOI: 10.1016/j.seppur.2015.06.017

[50] A. Apostolakis, S. Grigorakis, D.P.,Makris, Optimisation and comparative kinetics study of polyphenol extraction from olive leaves (*Olea europaea*) using heated water/glycerol mixtures. Separation and urification Technlology, 128, (2014), 89-95. DOI: 10.1016/j.seppur.2014.03.010

[51] V. Negro, G. Mancini, B. Ruggeri, D. Fino, Citrus waste as feedstock for bio-based products recovery: Review on limonene case study and energy valorization. Bioresource Technology, 214, (2016), 806-815. DOI:10.1016/j.biortech.2016.05.006

[52] M. Aissou, Z. Chemat-Djenni, E. Yara-Varon, , A.S. Fabiano-Tixier, F. Chemat, Limonene as an agro-chemical building block for the synthesis and extraction of bioactive compounds. Comptes Rendus Chimie, 20, (2017), 346-358 . DOI:10.1016/j.crci.2016.05.018

[53] R. Ciriminna, M. Lomeli-Rodriguez, P.D. Cara, J.A. Lopez-Sanchez, M. Pagliaro, Limonene: a versatile chemical of the bioeconomy.Chemical Communication, 97, (2014) 15288-15296 .DOI 10.1039/C4CC06147K

[54] M. Virot, V. Tomao, C. Ginies, F. Visinoni, F. Chemat, Green procedure with a green solvent for fats and oils' determination Microwave-integrated Soxhlet using limonene followed by microwave Clevenger distillation. J. Chromatogr A, 1196-1197, (2008), 147-152. DOI 10.1016/j.chroma.2008.04.035

[55] D.V. Bermejo, I. Angelov, G. Vicente, R.P. Stateva, M.R. García-Risco, G. Reglero, E. Ibañez, T. Fornari, Extraction of thymol from different varieties of thyme plants using green solvents. J Sci Food Agric **95**: (2014) 2901–2907. DOI:10.1002/jsfa.7031

[56] C. Tzia, G. Liadakis, eds., Extraction optimization in food engineering, Marcel Dekker, Inc, New York, 2003.

[57] S. Karaj, J. Müller, Optimizing mechanical oil extraction of Jatropha curcas L. seeds with respect to press capacity, oil recovery and energy efficiency, Ind. Crops Prod. 34 (2011) 1010–1016. doi:10.1016/j.indcrop.2011.03.009.

[58] L. Uhlenbrock, M.Sixt, J. Strube, Quality-by Design (QbD) processe valuation for phytopharmaceuticals on the example of10-deacetyl baccatin III from yew,Resource-EfficientTechnologies3(2017)137–143 http://dx.doi.org/10.1016/j.reffit.2017.03.001

[59] M. Sixt, J. Strube ,Systematic and Model-Assisted Evaluation of Solvent Based- or Pressurized Hot Water Extraction for the Extraction of Artemisinin from Artemisia annua L. Processes 2017, 5(4), 86; https://doi.org/10.3390/pr5040086

[60] M. Sixt, A. Schmidt, F. Mestmäcker, M. Johannes Huter, L. Uhlenbrock , J. Strube Systematic and Model-Assisted Process Design for the Extraction and Purification of Artemisinin from Artemisia annua L.—Part I: Conceptual Process Design and Cost Estimation Processes 2018, 6(9), 161; https://doi.org/10.3390/pr6090161

[61] F. Mestmäcker, A. Schmidt, M. Huter, M. Sixt, J. Strube Systematic and Model-Assisted Process Design for the Extraction and Purification of Artemisinin from Artemisia annua L.—Part III: Chromatographic Purification Processes 2018, 6(10), 180; https://doi.org/10.3390/pr6100180

[62] M. Johannes Huter, A. Schmidt, F. Mestmäcker, M. Sixt, J. Strube Systematic and Model-Assisted Process Design for the Extraction and Purification of Artemisinin from Artemisia annua L.—Part IV: Crystallization .Processes 2018, 6(10), 181; https://doi.org/10.3390/pr6100181

[63] ADEME (Agence de l'environnement et de la maîtrise de l'énergie), La chaleur fatale industrielle, Ademe Edition, Paris, (2015).

[64] A. Basile, M.M. Jiménez-Carmona, A.A. Clifford, Extraction of Rosemary by Superheated Water, J. Agric. Food Chem. 46 (1998) 5205–5209. **DOI:** 10.1021/jf980437e

[65] M. Bellumori, M. Innocenti, A. Binello, L. Boffa, N. Mulinacci, G. Cravotto, Selective recovery of rosmarinic and carnosic acids from rosemary leaves under ultrasound- and microwave-assisted extraction procedures, Comptes Rendus Chim.19 (2016) 699–706. DOI:10.1016/j.crci.2015.12.013

[66] L. Paniwnyk, H. Cai, S. Albu, T.J. Mason, R. Cole, The enhancement and scale up of the extraction of anti-oxidants from Rosmarinus officinalis using ultrasound, Ultrason. Sonochem. 16 (2009) 287–292. doi: 10.1016/j.ultsonch.2008.06.007.

[67] K. Assami, D. Pingret, S. Chemat, B.Y. Meklati, F. Chemat, Ultrasound induced intensification and selective extraction of essential oil from Carum carvi L. seeds, Chem. Eng. Process. Process Intensif. 62 (2012) 99–105. http://dx.doi.org/10.1016/j.cep.2012.09.003

[68] T. Allaf, V. Tomao, K. Ruiz, K. Bachari, M. ElMaataoui, F. Chemat, Deodorization by instant controlled pressure drop autovaporization of rosemary leaves prior to solvent extraction of antioxidants, LWT - Food Sci. Technol. 51 (2013) 111–119. DOI 10.1016/j.lwt.2012.11.07

[69] I.R. Kubra, L.J.M. Rao, Effect of microwave drying on the phytochemical composition of volatiles of ginger: Microwave drying of ginger, Int. J. Food Sci. Technol. 47 (2012) 53–60. **https://doi.org/10.1111/j.1365-2621.2011.02806.x**

[70] J. Hu, Z. Guo, M. Glasius, K. Kristensen, L. Xiao, X. Xu, Pressurized liquid extraction of ginger (Zingiber officinale Roscoe) with bioethanol: An efficient and sustainable approach, J.

Chromatogr. A. 1218 (2011) 5765–5773. DOI: 10.1016/j.chroma.2011.06.088

[71] V.G. Zuin, Circularity in green chemical products, processes and services: Innovative routes based on integrated eco-design and solution systems.Current opinion in Green and Sustainable Chemistry, 2, (2016), 40-44 https://doi.org/10.1016/j.cogsc.2016.09.008

[72] IEA (2016) Task 42; Implementing Strategies of Biorefineries in the BioEconomy. www.iea-bioenergy.task42-biorefineries.com.

[73] N. Rombaut, A.S. Tixier, A. Bily, F. Chemat, Green extraction processes of natural products as tools for biorefinery. Biofuels, Bioproducts and Biorefining, 8, (2014), 530-544 DOI 10.1002/bbb.1486

[74] F. Fava, G. Totaro, L. Diels, M. Reis, J. Duarte, O.B. Carioca, H.M. Poggi-Varaldo, B.S. Ferreira, Biowaste biorefinery in Europe: opportunities and research & development needs. New Biotechnology, 32, (2015), 100-108 DOI:10.1016/j.nbt.2013.11.003

[75] A.S. Matharu, E.M .de Melo, J.A. Houghton, Opportunity for high value-added chemicals from food supply chain wastes. Bioresources Technology, 215, (2016), 123-130. DOI: 10.1016/j.biortech.2016.03.039

[76] F. Chemat, M. Abert Vian, G. Cravotto, Green extraction of natural products: Concept and principles. Int. J. Mol. Sci. **13**, (2012) 8615 – 8627. DOI:10.3390/ijms13078615

[77] H. Letaief, Wine Making Process. In *Valorization of wine making by-products* (editor: Bordiga, M.) Taylor & Francis Group. (2016)

[78] I. Dávila, E. Robles, I. Egüés, J. Labidi, P. Gullón, The Biorefinery Concept for the Industrial Valorization of Grape Processing By-Products. In *Handbook of Grape Processing By-Products* (editor: Galanakis, C.M.) Elsevier Inc. (2017)

[79] G.A .Martinez, S .Rebecchi, D. Decorti, J.M.B. Domingos, A. Natolino, D. Del Rio, L. Bertin, C. Da Porto, F. Fava, Towards multi-purpose biorefinery platforms for the valorisation of red grape pomace: production of polyphenols, volatile fatty acids, polyhydroxyalkanoates and biogas. Green Chem, 18, (2016), 261-270. DOI: 10.1039/C5GC01558H

[80]. A. Teixeira, N. Baenas, R. Dominguez-Perles, A. Barros, E. Rosa, D.A. Moreno, C. Garcia-Viguera, Natural Bioactive Compounds from Winery By-Products as Health Promoters: A Review.Int. J. Mol. Sci, 15, (2014), 15638-15678 DOI:10.3390/ijms150915638

[81] M. Boukroufa, C. Boutekedjiret, L. Petigny, N. Rakotomanomana, F. Chemat, Bio-refinery of orange peels waste: A new concept based on integrated green and solvent free extraction processes using ultrasound and microwave techniques to obtain essential oil, polyphenols and pectin.Ultrason Sonochem, 24, (2015), 72-79. DOI:10.1016/j.ultsonch.2014.11.015

[82] J.A. Manthey, Potential Value-Added Co-products from Citrus Fruit Processing. In: *Biorefinery Co-Products* (edit.: Bergeron, C., Carrier, D.J., Ramaswamy, S.). John Wiley & Sons, Ltd. (2012)

[83] P. Putnik, J.M. Lorenzo, F.J. Barba, S. Roohinejad, A. Režek Jambrak, D. Granato, D. Montesano, D. Bursać Kovačević, Novel Food Processing and Extraction Technologies of High-Added Value Compounds from Plant Materials. Foods, 8, (2018), 106-122. DOI:10.3390/foods7070106

[84] A. Fidalgo, R. Ciriminna, D.Carnaroglio, A. Tamburino, G. Cravotto, G. Grillo, L.M. Ilharco, M. Pagliaro, Eco-Friendly Extraction of Pectin and Essential Oils from Orange and Lemon Peels. Sustainaible Chem. Eng., 4, (2016), 2243-2251. **DOI:** 10.1021/acssuschemeng.5b01716

[85] R. Ciriminna, N. Chavarría-Hernández, A.I. Rodríguez Hernández, M. Pagliaro, Pectin: A new perspective from the biorefinery standpoint. Biofuels, Bioprod. Bioref. 9, (2015) 368–377. **https://doi.org/10.1002/bbb.1551**

[86] D. Dawson, FDA Allows Cardiovascular Health on Olive Oil Labels. https://www.oliveoiltimes.com/olive-oil-health-news/fda-allows-cardiovascular-health-on-olive-oil-labels/66054 (2018)

[87] S. Souilem, A. El-Abbassi, H. Kiai, A. Hafidi, S. Sayadi, C.M. Galanakis, Olive oil production sector: Environmental effects and sustainability challenges. In *Olive Mill Waste. Recent Advances for Sustainable Management* (editor: Galanakis, C.M.) Elsevier Inc. (2017)

[88] M.J. Negro, P. Manzanares, E. Ruiz, E.Castro, M. Mercedes Ballesteros, The biorefinery concept for the industrial valorization of residues from olive oil industry. In *Olive Mill Waste. Recent Advances for Sustainable Management* (editor: Galanakis, C.M.) Elsevier Inc. (2017)

[89] J. Berbel, A. Posadillo, Review and Analysis of Alternatives for the Valorisation of Agro-Industrial Olive Oil By-Products. Sustainability, 10, (2018), 237-246. http://dx.doi.org/10.3390/su10010237

[90] F. Rodrigues, F.B. Pimentel, M.B.P.P. Oliveira, Olive by-products: Challenge application in cosmetic industry. Industrial Crops and Products, 70, (2015), 116-124. https://doi.org/10.1016/j.indcrop.2015.03.027

[91] G. Cravotto, F. Mariatti, V. Gunjević, M. Secondo, M. Villa, J. Parolin, G. Cavaglià, Pilot Scale Cavitational Reactors and Other Enabling Technologies to Design the Industrial Recovery of Polyphenols from Agro-Food By-Products, a Technical and Economical Overview. Foods, 7, (2018), 130-144. DOI:10.3390/foods7090130

[92] B. Barbaro, G. Toietta, R. Maggio, M. Arciello, M. Tarocchi, A. Galli, C.Balsano, Effects of the Olive-Derived Polyphenol Oleuropein on Human Health. Int. J. Mol. Sci. 15, (2014) 18508-18524. DOI:10.3390/ijms151018508

[93] S. Sahin, R. Samli, A.S.B .Tan, F.J. Barba, F. Chemat, G. Cravotto, J.M. Lorenzo, Solvent-Free Microwave-Assisted Extraction of Polyphenols from Olive Tree Leaves: Antioxidant and Antimicrobial Properties. Molecules, 22, (2017), 1056- 1069. DOI:10.3390/molecules22071056

[94] J.M. Romero-García, L. Niño, C. Martínez-Patiño, C. Álvarez, E. Castro, M.J. Negro, Biorefinery based on olive biomass. State of the art and future trends. Bioresource Technology, 159, (2014), 421-432. **DOI:** 10.1016/j.biortech.2014.03.062

[95] E. Ruiz, J.M. Romero-García, I. Romero, P. Manzanares, M.J. Negro, E. Castro, Olive-derived biomass as a source of energy and chemicals. Biofuels, Bioprod. Bioref. 11, (2017),1077–1094.

https://doi.org/10.1002/bbb.1812

[96] A. Schievano, F. Adani, L. Li Buessing, A. Botto, E.N. Casoliba, M. Rossoni, J.L. Goldfarb, An integrated biorefinery concept for olive mill waste management: supercritical CO_2 extraction and energy recovery. Green Chem, 5, (2015), 76-90 DOI: 10.1039/C5GC00076A

[97] M. Herrero, A. Cifuentes, E. Ibañez, Sub- and supercritical fluid extraction of functional ingredients from different natural sources: Plants, food-by-products, algae and microalgae: A review, Food Chem. 98 (2006) 136–148. DOI: 10.1016/j.foodchem.2005.05.058

[98] E. Ibañez, A. Kubátová, F.J. Señoráns, S. Cavero, G. Reglero, S.B. Hawthorne, Subcritical Water Extraction of Antioxidant Compounds from Rosemary Plants, J. Agric. Food Chem. 51 (2003) 375–382. DOI:10.1021/jf025878j

[99] S. Veillet, V. Tomao, F. Chemat, Ultrasound assisted maceration: An original procedure for direct aromatisation of olive oil with basil, Food Chem. 123 (2010) 905–911. DOI: 10.1016/j.foodchem.2010.05.005

[100] Y. Li, A.S. Fabiano-Tixier, V. Tomao, G. Cravotto, F. Chemat, Green ultrasound-assisted extraction of carotenoids based on the bio-refinery concept using sunflower oil as an alternative solvent, Ultrason. Sonochem. 20 (2013) 12–18. DOI:10.1016/j.ultsonch.2012.07.005

[101] J.L. Luque-García, M.D. Luque de Castro, Water Soxhlet Extraction Assisted by Focused Microwaves: A Clean Approach, Anal. Chem. 73 (2001) 5903–5908. **DOI:** 10.1021/ac0155815

[102] Règlement (CE) N° 1907/2006 du Parlement européen et du Conseil, (2006).

[103] M. Siegrist, B. Sütterlin, Importance of perceived naturalness for acceptance of food additives and cultured neat, Appetite, 113 (2017), 320-326 DOI:10.1016/j.appet.2017.03.019

[104] Direction Générale de la Concurrence, de la Consommation et de la Répression de Fraudes (DGCCRF), Note d’information n°2009-136 (communicable au sens de la loi du 17 juillet 1978), (2009).

[105] COSMOS-standard AISBL, COSMOS-Standard, Cosmetics organic and natural standard, (2013).

[106] ECOCERT GREENLIFE, Référentiel ECOCERT, Cosmétiques écologiques et biologiques, (2012).

[107] H. Verhoog, E. Lammerts Van Bueren, M. Matze, T. Baars, The value of 'naturalness' in organic agriculture, NJAS- Wageningen Journal of Life Science, 54 (2007), 333-345

[108] H. Cui, T. Wang, Z. Shen, Removal of Trace Heavy Metals from a Natural Medicine Material by Supercritical CO_2 Chelating Extraction, Ind. Eng. Chem. Res.,40, (2001) 3659–3663.

[109] C. Valderrama, X. Gamisans, X. De Las Heras, A. Farrán, J.L. Cortina, Sorption kinetics of polycyclic aromatic hydrocarbons removal using granular activated carbon: Intraparticle diffusion coefficients, J. Hazard. Mater., 157 (2008) 386–396.

[110] G. Rebitzer, T. Ekvall, R. Frischknecht, D. Hunkeler, G. Norris, T. Rydberg, W.P. Schmidt, S. Suh, B.P. Weidema, D.W. Pennington, Life cycle assessment: Part 1: Framework, goal and scope definition, inventory analysis, and applications, Environ. Int., 30,(2004) 701–720.

Table 1. Some recent studies of phenols extracted from natural resources using SWE.

Raw material	Target compound	Optimal operating conditions	References
Mango peels	Total phenols	180 °C, 90 min, solid to water ratio 1:40	[27]
Uva ursi herbal dust	Total phenols and total flavonoids	151.2 °C, 10 min, 1.5% HCl	[28]
Wild garlic (*Allium ursinum* L.)	Total phenols and total flavonoids	180.92 °C, 10 min, added acidifier 1.09%	[29]
White grape pomace	Total phenols	210 °C, 100 bar, 30 min	[30]
Winter savory (Satureja montana L.)	Total phenols and total flavonoids	220 °C, 20.8 min, 30 bar	[31]
Spent coffee grounds (*Coffea arabica* L.)	Total phenols	177.00 °C, 55 min, 50 bar	[32]
Ginger	Gingerol	130ºC, 20 min, 2 bar	[33]
Black tea	Myrcetine and Quercetin* Kampherol**	170 °C, 15 min, 101 bar* 200 °C, 15 min, 101 bar**	[34]
Celery powder	Myrcetine and Quercetin* Kampherol**	170 °C, 15 min, 101 bar* 200 °C, 15 min, 101 bar**	[34]
Ginseng leaf	Myrcetine and Quercetin* Kampherol**	170 °C, 10 min, 101 bar* 200 °C, 15 min, 101 bar**	[34]
Tumeric rhizomes (*Curcuma longa* L.)	Curcumin	140 °C, 10 bar, 14 min	[35]

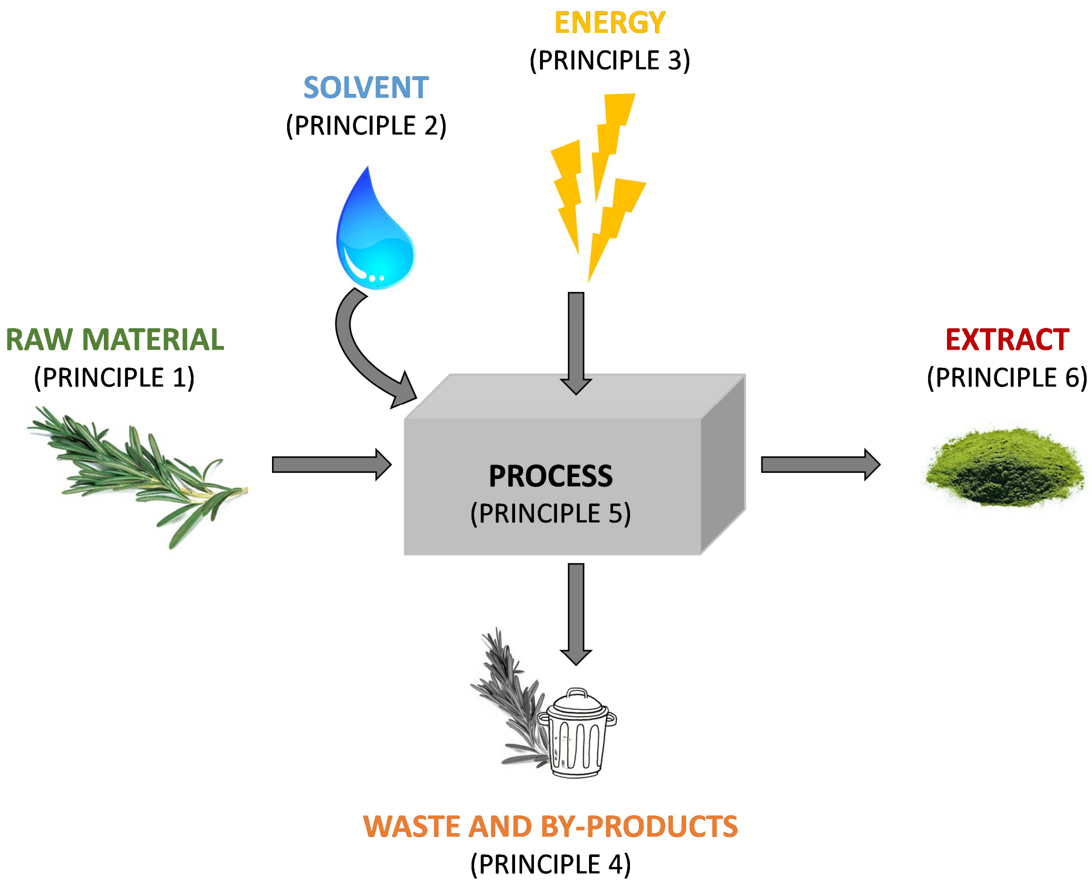


Figure 1: Essential inputs and outputs of extraction process related to the six principles of green extraction.

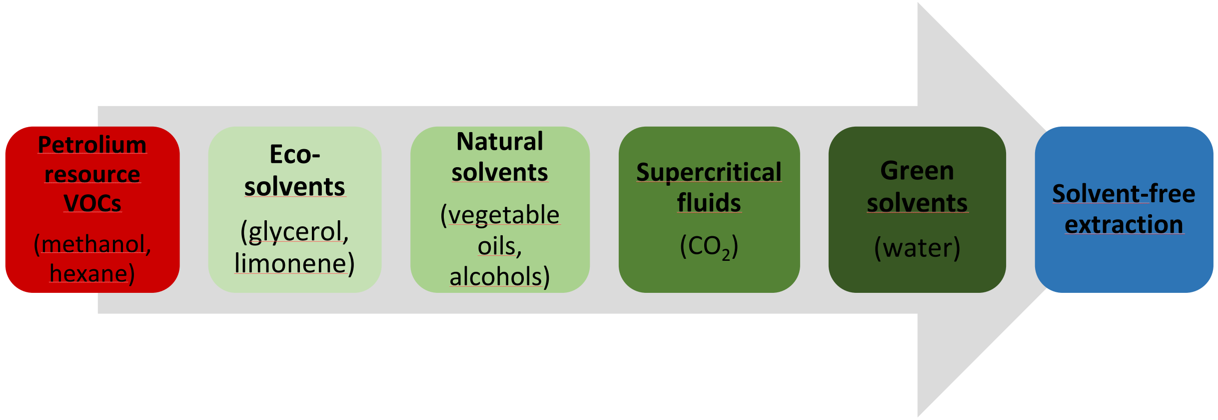
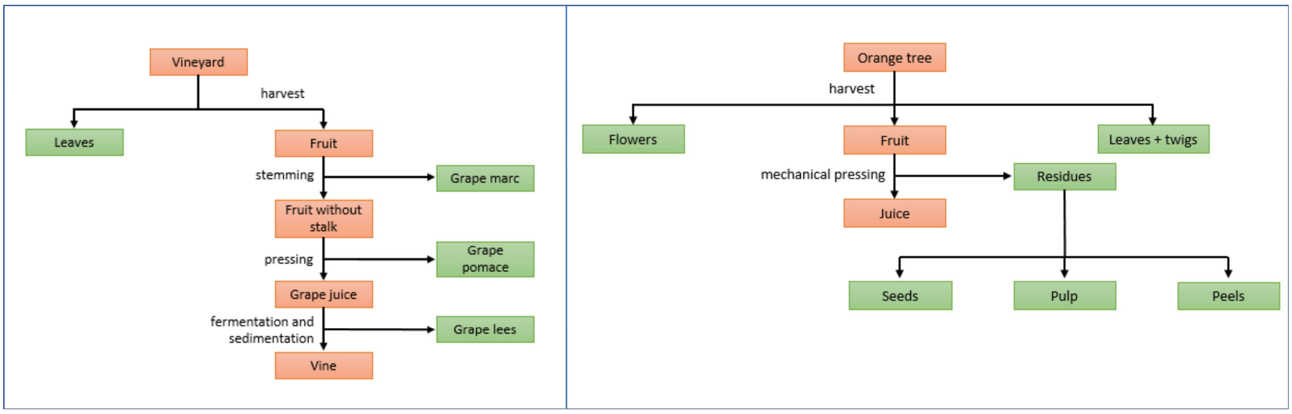


Figure 2. From petroleum to alternative and green solvents

Figure 3. Assessment of available innovative processes for green extraction.

1



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3 **Figure 4.** Simplified scheme of by-products generated during wine and orange fruit processing

4

5

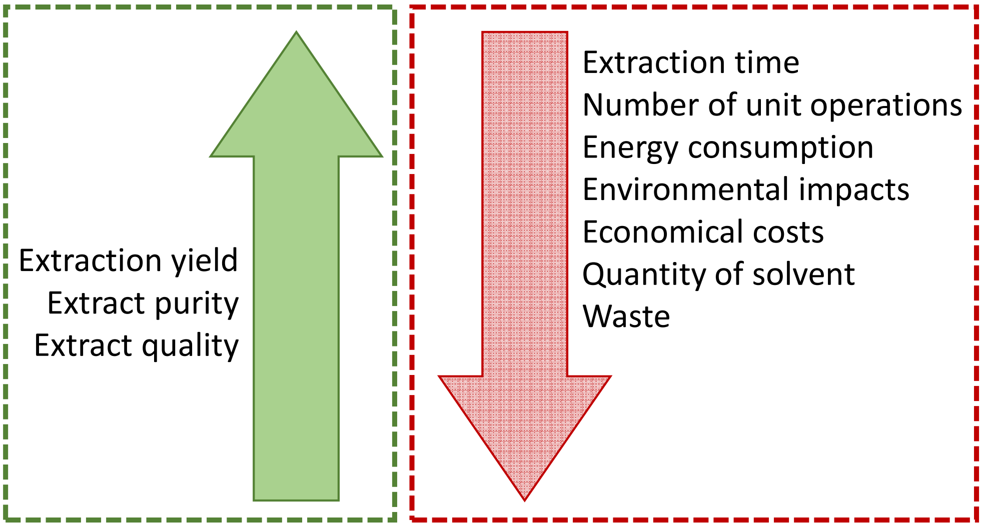
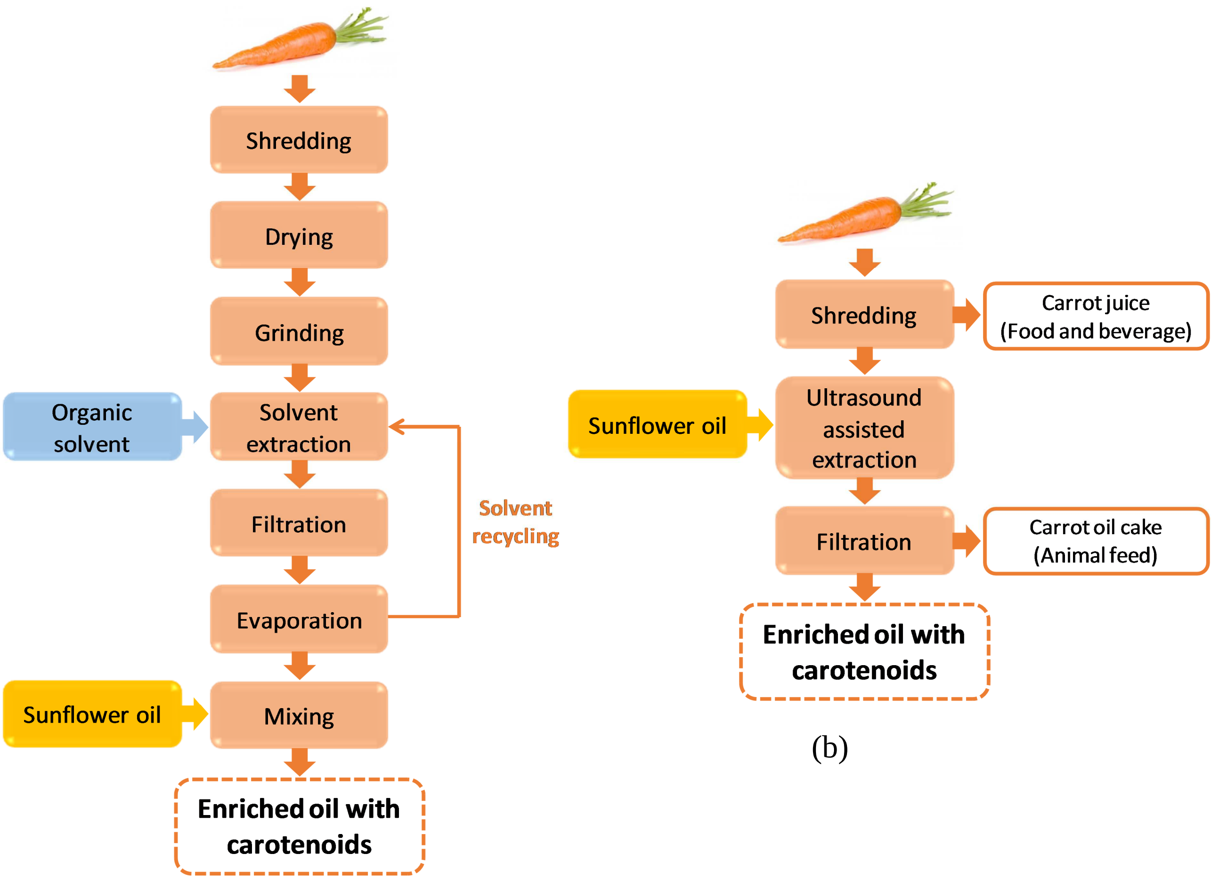


Figure 5. Principle of intensification of extraction process



(a)

Figure 6. Processing procedures to obtain enriched oil with carotenoids by (a) conventional solvent extraction and (b) ultrasound assisted extraction

Figure 7. Examples of labels with naturalness values.

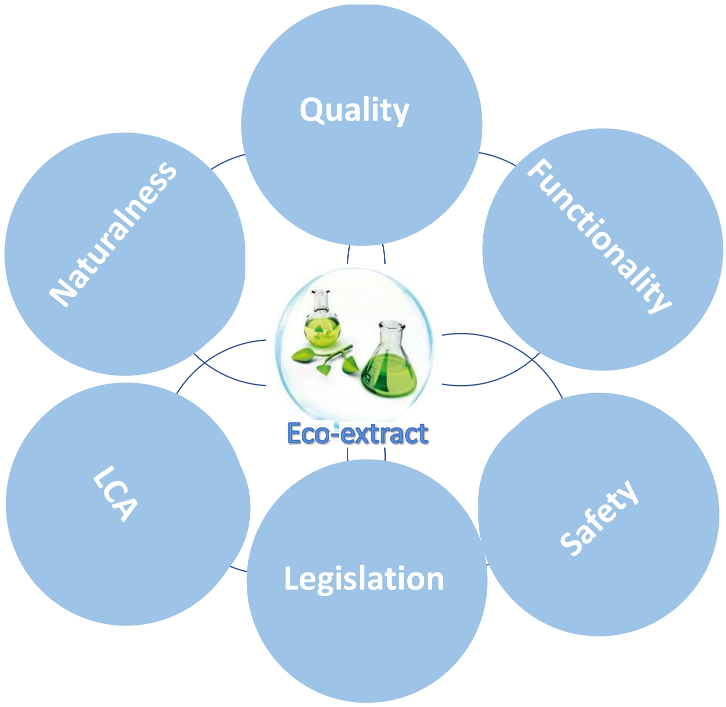


Figure 8. Characteristics defining an “eco-extract”.

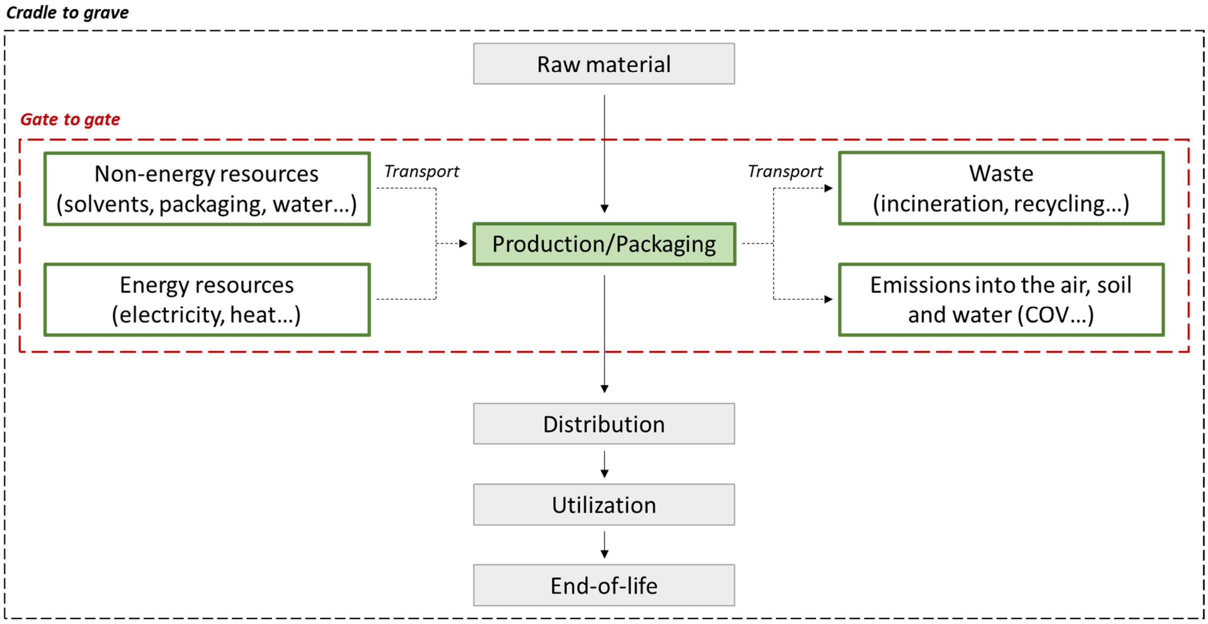


Figure 9. “Gate to gate” approach in Life Cycle Assessment methodology.

Highlights

Recent advances in green extraction of natural products are detailed.

Green extraction techniques enhances processing yield, economy and impacts

Green extraction techniques as efficient tools for plant-based chemistry.