

Extraction and purification of high added value compounds from by-products of the winemaking chain using alternative/non-conventional processes/technologies

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Abstract

Grape byproducts are today considered as a cheap source of valuable compounds since existent technologies allow the recovery of target compounds and their recycling. The goal of the current article is to explore the different recovery stages used by both conventional and alternative techniques and processes. Alternative pre-treatments techniques reviewed are: ultrasounds, pulsed electric fields and high voltage discharges. Additionally, non-conventional solvent extraction under high pressure, specifically, supercritical fluid extraction and subcritical water extraction are discussed. Finally alternative purification technologies, for example membrane processing were also examined. The intent is to describe the mechanisms involved by these alternative technologies and to summarize the work done on the improvement of the extraction process of phenolic compounds from winery by-products. With a focus on the developmental stage of each technology, highlighting the research need and challenges to be overcome for an industrial implementation of these unitary operations in the overall extraction process. A critical comparison of conventional and alternative techniques will be reviewed for the pre-treatment of raw material, the diffusion of polyphenols and the purification of these high added value compounds. This review intends to give the reader some key answers (costs, advantages, drawbacks) to help in the choice of alternative technologies for extraction purposes.

Key words

Extraction, purification, grape by-products, high added value compounds, non-conventional technologies

1. Introduction

The valorization of winery waste products is very promising, since grape is one of the largest produced fruit crops with an annual world production of 64 million tons in 2014 (FAOSTAT, 2014). About 80% is used for winemaking and it has been estimated that 13 to 20% of by-products, which represents about 5-8 million tons of potentially exploitable matter, are generated after the winemaking process (Pinelo et al., 2005; Arvanitoyannis et al., 2006; Jackson, 2008). Other estimations report higher values up to 14.5 million tons solely in Europe (Torres et al., 2001; Peralbo-Molina et al., 2013). This represents unquestionably an enormous amount of matter from which high added value components could be extracted. Solid grape wastes are particularly rich in polyphenols, whose use extends to applications in various fields, including cosmetic, nutraceutical, chemical and food industries. Over the last years, polyphenols have attracted a growing interest for their potential health benefits in preventing heart diseases and cancers (Craft et al., 2012; Kähkönen & Heinonen, 2003; Quideau et al., 2011; Stintzing et al., 2002). Their extraction from winery waste and their following purification are of special interest to produce extracts with high added value.

Phenolic compounds are usually extracted by classical extraction procedure (Figure 1). The natural variability of raw material and the pre-transformation processes (drying, grinding, etc.) could be determinant for the quantity and the composition of extract (Meireles, 2008). For instance, high temperatures can lead to denaturation of targeted compounds and grinding leads to a significant increase of undesired components during extraction. Thus, conventional pre-transformation processes decrease the selectivity and/or the efficiency of the extraction process.

The selectivity of the extraction processes also depends on the molecular affinity between solvent and solute during the solid-to-liquid diffusion step (Cowan, 1999). However, toxicity, environmental safety, and financial feasibility should also be considered in the selection of a solvent for the extraction of high added value compound. Towards the end of the process, a purification step may be required to obtain extracts with high purity of phenolic compounds. Resin adsorption is commonly used at industrial scale (Silva et al., 2007; Soto et al., 2011). The major drawback of this technique is the use of a large amount of solvent noticeably during polyphenols desorption, which need to be further evaporated.

Losses of some compounds, low production efficiency, time- and energy-consuming procedures (prolonged heating and stirring, use of large volumes of solvent...) may be encountered using this conventional extraction procedure. Recent trends in extraction techniques have largely focused on finding solutions that minimize the use of solvent and energy. For these purposes, alternative techniques have been deeply studied to enhance the overall yields in phenolic compounds and to decrease the operational costs of the process. These techniques include:

- Alternative pre-treatments techniques: ultrasounds, pulsed electric fields and high voltage discharges,
- Non-conventional solvent extraction under high pressure: supercritical fluid extraction and subcritical water extraction and,
- Alternative purification technologies, such as membrane processing.

Although lots of experimental studies particularly focused on improving the overall extraction process from solid winery by-products, none of these alternative technologies are currently used at industrial scale for this application. This paper intends to describe the mechanisms involved by above selected alternative technologies and to summarize the work done on the improvement of the extraction process of phenolic compounds from winery by-products. This review was focused on the above-mentioned techniques. However there are more options to extract polyphenols from winemaking by-products than the ones considered, such as pulsed ohmic heating (Darra et al., 2012), microwave assisted extraction (Delgado-Torre et al., 2012; Liazid et al., 2011; Zhao et al., 2008), accelerated solvent extraction (Monrad et al., 2010a; Rajha et al., 2014) and the use of hydrotropic solvents (Rajha et al., 2015). In this review, the contribution focuses on the developmental stage of each technology, highlighting the research need and challenges to be overcome for an industrial implementation of these unitary operations in the overall extraction process. A critical comparison of conventional and alternative techniques will be described for the pre-treatment of raw material, the diffusion of polyphenols and the purification of these high added value compounds. This review intends to give the reader some key answers (costs, advantages, drawbacks) to help him in the choice of alternative technologies for extraction purposes. The focus is on work done until the year 2013, with the most recent works from the year 2014 and 2015 mentioned.

2. Pre-treatment of grape by-products for the enhancement of mass transfer phenomena: conventional and alternative techniques

Phenolic compounds exist in plants enclosed in particular structures such as the vacuoles of plant cells and lipoproteins bilayers (Agati et al., 2012). In intact cells, the membrane envelope

restricts the exchange between the intracellular media and the surrounding solvent. Consequently, conventional solvent extraction techniques such as maceration or diffusion require long extraction time, due to the slow diffusion of solvent and solute through the solid (Gamse, 2002). Thus, the degradation of cell-wall and of intracellular components is a fundamental step to improve the release of these compounds from the grape tissues. Extraction processes can be enhanced by several pre-treatments of the plant materials that are able to physically damage the cells, such as: grinding, pulsed electric field, high voltage electric discharges and ultrasound.

2.1. Grinding

Grinding is the most conventional pre-treatment technique and is currently used in the extraction industry to shorten the time of diffusion and enhance the yield of targeted bio-compounds. The mechanical action induced by grinding leads to an increase of the exchange surface. However, grinding also leads to the overheating of the plant matrix. Two phenomena are responsible of this released heat:

- Release of energy caused by the fracturing of the matrix,
- Release of energy due to overgrinding of the matrix (Bhattacharya, 2014).

Phenolic compounds, and noticeably anthocyanins, are particularly thermosensitive and can be degraded or lose their functionality (Khanal et al., 2010).

On the other hand, the type of plant matrix, and particularly its moisture content, affects the electrical energy requirement, the specific energy consumption and the equipment to be used (Chakkaravarthi et al., 1993). Two types of grinding processes can be used in the food industry: dry and wet grinding. A previous study demonstrated that specific energy consumption varied

between 420 and 800 kJ/kg of raw rice using dry grinding, while about 14,000 kJ/kg were required in the case of wet grinding (water-to-rice ratio = 2) (Ngamnikom & Songsermpong, 2011). Consequently, a preliminary drying step, which is associated with matrix heating, is often required to facilitate the grinding and reduce its associated cost (Ngamnikom & Songsermpong, 2011; Walde et al., 2002).

Finally, increased difficulties during the filtration and purification steps due to small particles in suspension in the solvent are another limitation for the use of grinding in the extraction manufactories.

Emerging technologies for the physical alteration of raw material (i.e. pulsed electric fields, high voltage electric discharges and ultrasounds) are based on non-thermal concepts. These three technologies can physically affect the permeability of the cell by different mechanisms (Boussetta & Vorobiev, 2014; Chemat et al., 2011; Toepfl, 2012; Vorobiev & Lebovka, 2009).

2.2. Pulsed electrical field (PEF) assisted extraction

Electroporation phenomena

When subjected to an external electric field, the charge accumulation on the membrane surfaces induces the increase of transmembrane potential of the cell membrane, initiating pore formation (Barbosa-Cánovas, 1999). Typically, electroporation phenomena requires some threshold value of transmembrane potential around 0.5 - 1.5 V (Weaver & Chizmadzhev, 1996). Above the critical value of transmembrane potential, the expansion of pores present in weak

areas of the membrane will induce drastic increase of permeability (Knorr et al., 2001; Zimmermann, 1986) and will facilitate the leakage of intracellular compounds (Donsì, Ferrari, & Pataro, 2010; Eugène Vorobiev & Lebovka, 2008). Thus, Pulsed Electric Field (PEF) treatment increases transmembrane transport of molecules (Kotnik et al., 2012; Vorobiev and Lebovka, 2008, 2009). For cellular tissues of 60-120 μm in diameter, initiation of pore formation can be achieved using electric field strengths of 0.1 - 0.5 kV/cm and treatment times of very short duration (within 10^{-4} - 10^{-2} s) (Pakhomov et al., 2010) without any significant temperature increase (Fincan & Dejmek, 2002; Lebovka et al., 2002).

Pulsed electric field pre-treatment of winery by-products

PEF treatment prior to conventional extraction allowed a better recovery of phenolic compounds from different winery by-products (**Table 1**). In most of these studies, the raw materials were submerged into water in order to improve electrical contacts between electrodes. Treatment with liquid-to-solid ratio above 5 required high electric field strength (i.e. $E > 13$ kV/cm) to be effective for the enhancement of polyphenols extraction. As a consequence, specific energy consumptions were relatively high (i.e. $272 < W < 762$ kJ/kg of treated raw material). On the contrary, pre-treatment by PEF combined with an accurate densification of wet pomace or wet skins can be achieved at lower electric field strengths (i.e. $E \approx 1.2$ kV/cm) and lower energy requirements (i.e. $18 < W < 30$ kJ/kg of treated raw material). The treatment of compacted wet winery by-products requires less output current, which can be advantageous for the industrial implementation of PEF (Brianceau, et al., 2014). Pulse forms used were of different shape (monopolar, bipolar or exponential). However, no comparison of the effect of

pulse shape on the extractability of phenolic bio-components is available in the existing literature.

Interestingly, a previous study showed that PEF treatment causes irreversible perforations in the cell wall of the outer hypodermis and distention of the fiber cell wall polysaccharides at the inner hypodermis (Cholet et al., 2014). This electroporation phenomenon may allow the specific recovery of anthocyanins that are particularly located in the upper cell layers of the hypodermis. For instance, High Intensity Pulsed Electrical Field (Hi-PEF) treatment of fermented grape pomace (13.3 kV/cm, $W = 272$ kJ/kg) allowed the selective recovery of anthocyanins and the production of extracts with a high ratio anthocyanins/Total Phenolic Compounds (TPC). This reflects an increase of 40% that cannot be achieved by conventional extraction procedure, such as grinding combined to diffusion (ratio anthocyanins/TPC < 5%) (Barba et al., 2015). Moderate PEF treatments ($E < 3.0$ kV/cm, $W < 20$ kJ/kg) were also effective in enhancing anthocyanins extraction from grape skins (+ 17%) (Corrales et al., 2008) and grape pomace (+ 19%) (Sylène Brianceau et al., 2014). Consequently, PEF can replace conventional pre-treatments of grape by-products (e.g. dehydration and grinding), which have impacts on product quality and are more energy consuming, with the combined objectives of cost reduction and selectivity of extraction.

Scale-up of the technology/Stage of development

Based on existing concepts, and noticeably on sucrose extraction from sugar beets at industrial scale (Sack et al., 2010; Schultheiss et al., 2003; Toepfl, 2012), the pre-treatment of grape by-products by PEF should be feasible at larger scale (pilot and industrial scale). Progress

in the development of continuous flow treatment chambers for PEF processing have allowed the treatment of material that cannot be pumped (solid products) using belt or rotating systems (Vorobiev & Lebovka, 2012). Moreover, some recent developments of pulsed power systems, which are usable for continuous delivery of high amounts of electrical energy and high electric field strengths and suitable for food industry applications, have allowed the scale-up of the technology (Toepfl, 2012).

Research needs and challenges

While electroporation devices for minimally processed fruits and vegetables are already in operation (Puértolas et al., 2012), the electroporation devices for extraction of valuable components from grape by-products still require some research and development prior to any reliable operation in an industrial environment.

At the microscopic scale, questions still remain regarding the effect of electric pulses on the cell structure of the plant material and on the targeted bio-components. For instance, it was demonstrated that PEF treatment can modify molecular interactions between intracellular components (Cholet et al., 2014) and induce a rupture of polymer chains (decondensation of the tannins) (Delsart et al., 2013). Further studies might be of importance to evaluate the effect of PEF treatment on the properties of the targeted molecule (bioavailability, functionality, taste...) before using these extracts in food, oenological or nutraceutical applications.

In order to implement the PEF processing step into existing processes in a distillery, a winery or an extracts manufactory, a systemic/integrative approach will be required considering the diversity of raw material to be treated (i.e. pomace, skins, stems, seeds and vine shoots):

- Depending on the grape by-product to be treated, the peak voltage required, the peak current (which depends on product conductivity, on the minimum treatment chamber cross section and on the electrical resistance of the chamber), the average power (dependent on the processing capacity (kg or tons /hour...)) and on the pulse waveform (exponential decay or rectangular pulses) can vary substantially, which renders the design of a power supply for multiple applications challenging.

- The suitability of the treatment chamber may be affected by the raw materials to be treated, most noticeably the materials' pumpability that is critical for a continuous treatment at an industrial scale.

2.3. High voltage electrical discharges (HVED) assisted extraction

Principles and mechanisms: The first step of HVED is the formation and the propagation of a streamer, which is composed of thin ionized vapor channels, from a needle electrode (pre-breakdown phase). The second phase occurs when the streamer reaches the plate electrode (breakdown phase). These two phases are accompanied by different secondary phenomena such as propagation of pressure shock waves in the surrounding media, emission of UV light, gas bubbles cavitation and chemical reactions generating reactive species (Boussetta & Vorobiev, 2014; Jiang et al., 2014; Joshi et al., 1995). At the macroscopic level, the application of electrical discharges on different wine by-products (grape seeds, grape pomace...) results on the fragmentation of the particles (Boussetta et al., 2013). Depending on the matrix and after effective discharge treatment, the size reduction of the particles treated by electrical discharge is rather similar to that obtained after grinding the product (Boussetta et al., 2012).

HVED-assisted extraction of valuable bio-compounds from winery by-products: Electrical discharges have been successfully applied at both laboratory (1 L) and pilot (35 L) scales, in batch, for the enhancement of polyphenols extraction from winemaking by-products (**Table 2**). At the macroscopic level, the treated grape by-products were clearly fragmented after the application of electrical discharges. The increase of the exchange surface promotes the release of non-cell-wall phenolic components and enhances the ethanol transport into cells leading to an increase of phenolic compounds recovery (Boussetta et al., 2011; Brianceau et al., 2015). Moreover, the highly turbulent conditions induced by HVED accelerate the convection of these components from particles to the surrounding medium.

In general, specific energy consumption ranged from 32 kJ/kg and 254 kJ/kg of treated raw material to achieve interesting enhancement of phenolic compounds extraction. At laboratory scale, lignocellulosic biomass (i.e. grape stems, vine shoots) required the highest energy input (> 190 kJ/kg), probably because these biomasses are more resistant to electric discharges than grape skins or seeds.

However, the choice of effective HVED treatment time should be accurately evaluated, as excessively prolonged treatment may deteriorate phenolic compounds. This deterioration of phenolic compounds, and particularly of catechin, epicatechin, quercetin-3-O-glucoside and kaempferol-3-O-glucoside, has been observed above 80 kJ/kg of HVED treatment on grape pomace (Boussetta et al., 2011). Procyanidin B2 from grape stems showed similar behavior above 122 kJ/kg of energy input (Brianceau et al., 2015). Concomitant mechanical and chemical actions induced by the process may be responsible for these observations. Indeed, free radicals

can be formed via the thermal dissociation of water during electrical discharge treatment. Under these extreme conditions, antioxidant capacity can be affected (Joshi et al., 1995).

Stage of development, research needs and challenges

Despite recent research of the effects of HVED for the enhancement of the extraction of phenolic compounds, particularly from winery by-products, this technology is still at its early stage of development. Further research is needed to make this technology feasible at the commercial level.

The detailed mechanism of the establishment of electric discharges in water is still not fully understood. There are two primary principal competing schools, namely, an electron multiplication theory and a phase change mechanism breakdown theory (Jiang et al., 2014) but until now, there is no consensus on the physical principles involved during this process. Moreover, the evaluation of bioavailability, functionality and/or the taste of the extracts obtained using this process might be of value before oenological or nutraceutical applications.

To intensify the mass transfer phenomena, electric discharges in water have been applied using electrodes with point-to-plane geometry. This geometry is not completely suitable for industrial applications because only restricted volumes can be treated due to low electrical discharges zone. Moreover, identification and application of electrode materials that can provide longer time of operation and lower metal migration would be of value as the lifetime of the needle is rather limited. Another key aspect for the successful application of HVED-assisted extraction is the design uniformity and the processing capacity of the treatment chamber. At this

stage of development, HVED treatment would only be dedicated to small batch production of extract.

2.4. Ultrasound (US) assisted extraction

Principles and mechanisms

The major effects of ultrasounds (from 20 kHz to 10 MHz) in a liquid medium are attributed to cavitation phenomena. Cavitation is the result of a physical process inducing the creation, the expansion and the implosion of microbubbles, which are formed from gases initially dissolved in the liquid. Held together by attractive forces, molecules are displaced as the ultrasound wave passes through the liquid medium. The sound wave acts as a piston on the surface of the medium, thus inducing cycles of compression phase followed by rarefaction phase. The distance will increase between the molecules of the medium during the rarefaction phase (McClements, 1995). If the power is sufficiently high, this distance will reach a critical value, the liquid would breakdown and voids, or cavitation bubbles, can be generated into the liquid (Chemat et al., 2011). During a compression cycle, upon reaching critical point, bubbles created collapse with temperature and the pressure estimated to be up to 5000 K and 2000 bars. This released temperature and pressure creates microjets pointed towards the solid surface. This leads to destruction of the cell walls of the plant matrix allowing an increase in extraction yields (Vinatoru, 2001).

US-assisted extraction of valuable bio-compounds from winery by-products

Ultrasounds can be applied for extraction purposes in two ways: directly to extraction media via an ultrasonic probe, or indirectly through the walls of the extraction media container using a water bath. Both types of apparatus operating at frequencies between 25 and 55 kHz are used at laboratory scale for the enhancement of phenolic compounds extraction from winery by-products (**Table 3**). Optimal US treatment times varied between 25 min and 60 min for phenolic compounds extraction whatever the US device used. This corresponds to specific energy consumption ranging from 187.5 kJ/kg and 4,580 kJ/kg of treated grape by-products. For non-lignocellulosic material (i.e. grape pomace, skins and seeds), US bath is more energy consuming ($W > 4,000$ kJ/kg) than titanium US probe ($W < 1,530$ kJ/kg).

In both cases, ultrasonic systems are composed of a transducer, which converts electrical energy into sound energy by vibrating mechanically at ultrasonic frequencies, generating ultrasounds (Povey & Mason, 1998). The acoustic intensity (W/cm^2), which is determined as the ratio between the ultrasonic power applied and the emitter surface of the probe system given by common ultrasonic bath at laboratory scale is generally low (1 -- 5 W/cm^2) in order to avoid cavitation damage to the tank wall. The acoustic intensity provided by a probe is at least up to 100 times greater than the one supplied by the bath (Santos & Capelo, 2007), one of the major limitation being the cavitation erosion of the surface of the emitter. This major difference makes each system devoted for a different set of applications, depending noticeably on the operation cost and on the sensibility to degradation of the molecules to be extracted. Thus, US

bath should be more adapted for laboratory extraction of phenolic compounds from grape by-products, while US probe can be used at larger scale.

It is generally agreed that ultrasound has weak effects on the stability of extracted compounds. Nevertheless, specific attention should be paid to the stability of extracted component after a long exposure to ultrasonic irradiation. However, long exposure to ultrasonic irradiation, in some cases, may degrade phenolic compounds particularly anthocyanins (Pingret et al., 2013).

Scale-up of the technology/Stage of development

Based on the analysis of different advancements in the large scale operation, the development of continuous reactors and use of multiple transducers (Shirsath et al., 2012) with a possibility of multiple frequency operation (Gogate & Pandit, 2004) is the key to effective large scale operation and could easily be used for the treatment of different matrices, including grape by-products (Gogate et al., 2011). Moreover, some continuous flow systems have been developed for both laboratory and pilot plant scale. Continuous extractors consisting in belt or screw conveyors have been equipped with ultrasound (Dolatowski et al., 2007). US technology for extraction purposes is already in use at industrial scale. The main matrices of ultrasound-assisted extraction are seeds and herbs for food and cosmetic additives application (Chemat et al., 2011). The high polyvalence of the existing concepts in the ultrasound technologies should allow an easy scale up for the intensification of the extraction of biomolecules from the different matrices of grape by-products.

Research needs and challenges

One of the difficulties reported in the literature is the non-standardized methodologies and control parameters. Thereby, the current challenge is to establish conditions in terms of characterization of sound field, probe types and sample volumes aiming at the techno-economical optimization prior to industrial exploitation (Rastogi, 2011). Another problem hampering the effective operation at commercial scale is from the field of material science and deals with possible erosion of transducer material with continuous use, leading to a decreased transfer of energy and also need for frequent replacements (Coupland, 2004). Thus, further research needs to be directed in terms of development of high power ultrasonic (HPU) transducers (Patist & Bates, 2011), with higher power capacity, efficiency, radiating surface area and more sophisticated control system. Theoretical work is indeed required for efficient optimization of the large scale design of the sonochemical reactor.

2.5. Comparison of pre-treatment processes

Several studies performed at laboratory scale have aimed at comparing the pre-treatment techniques described above on the recovery of phenolic compounds from grape by-products. The results evidenced that HVED was the less energy consuming process, followed by PEF and US, and the most efficient for the recovery of total phenolic compounds (Barba et al., 2015; Rajha, et al., 2014). However, HVED and US were less selective than PEF regarding the specific recovery of anthocyanins (Barba et al., 2015; Corrales et al., 2008).

Figure 1 compares the specific energy required by each technology for the pre-treatment of the winery by-products. The use of alternative technologies would allow an interesting decrease

of the energy consumption, compared to conventional pre-treatment by grinding. The location of targeted compounds with respect to tissue structures seems to be a key issue in the choice of the pre-treatment to be applied. Based on the previous observations, table 4 resumes the advantages and drawbacks of the different pre-treatments.

The pre-treatment of the grape by-products is usually followed by a diffusion step that allows the recovery of the solutes in a suitable solvent. New techniques based on high pressure/high temperature promised to reduce diffusion costs by reducing the amount and the type of solvent used, the diffusion time and by enhancing the extraction yields.

3. Solid-to-Liquid extraction (SLE) of high added value compounds:

3.1. Conventional Extraction technique: Low pressure extraction using organic solvents

Principles and mechanisms: A well-established technology, solid-to-liquid extraction is the conventional technique that allows polyphenol components to be removed from the grape by-products matrix using a solvent. Molecular affinity between the solvent and the solute depends on the extracting power of the solvent (Cowan, 1999).

Several interfering parameters are involved for quantitative extraction of phenolic compounds from grape by-products. Work that applied a single-stage solvent extraction, is presented in Table 5. These literature works aimed at optimization of several extraction process parameters such as: type of solvent, time, temperature of extraction and pH of the extraction medium liquid-to-solid ratio.

Solvent extraction of valuable bio-compounds from winery by-products: Water and ethanol are both accepted as biocompatible solvents, renewable and low-cost resources existent in wineries and distilleries. By increasing the amount of ethanol in water, this has lead to an increased total polyphenol extraction (Spigno et al., 2007). The optimum extraction was reached through the use of an ethanol/water solution having a percentage of ethanol between 50 and 70% (Bozan et al., 2006). Later studies confirmed the results and specified a 66% ethanol solution (Rajha, et al., 2014).

The presence of an acid or a base in the solvent enhances the degradation of the plant material, increasing the extraction capacity from the matrix as well as the solubility of these bioactive compounds. Increasing the acidity of the extraction solvent, lead to the denaturation of the cell membrane, which simultaneously dissolves anthocyanin, and stabilizes them (Ju & Howard, 2003). To obtain the best yields of anthocyanin extraction, weak organic acid, or low concentration strong acid have been used. An acidic pH, between 1.0 and 2.5, increases both total yields and phenolic contents. For example 0.1% HCl, 1% acetic acid, and tartaric acid have been often used in the solid-liquid extraction process (Hashim et al., 2013; Makris, Boskou, & Andrikopoulos, 2007). In addition, sulfured water has also been proposed as an extraction solvent seeking a reduction of the use of organic solvents (Ju & Howard, 2003). However, excessive acidity of the medium leads to hydroxylation of labile, acyl, and sugar residues during the concentration step (Pekić et al., 1998).

The recovery of phenolic compounds is also influenced by time and temperature. An increase in temperature can cause a higher solubility yet this is accompanied by degradation of polyphenols

due to their oxidation. For example several studies have shown an increase of total polyphenol yield at 50°C in comparison to room temperature extraction (Bozan et al., 2008; Guerrero et al., 2008). However, an increase in the temperature should be coupled by shorter extraction times, lower than 8h, to avoid polyphenols degradation and/or polymerization.

Stage of development, research needs and challenges: Several of these techniques are used for laboratory application and are currently the benchmark for industrial extraction since they are simple, inexpensive and do not require special equipment or qualified personnel. Leading to classifying this extraction as a mature technique, with full industrial practice with little technological risk. Additionally, to cope with the up-scale to industrial processes there is a sufficient variety of large-scale equipment available.

However this mature technique has its own drawbacks. Since large amounts of organic solvents involved during extraction, there is a prominent need for their elimination without traces before commercialization of the extract. Also solvent regeneration e.g., distillation or evaporation increase the utilized energy. Furthermore this technique has low extraction efficiency and a long extraction time. Compared to this technique several selective extractions such as subcritical and supercritical fluid extraction have proven their effectiveness.

3.2. High-pressure extraction

3.2.1. High temperature and high-pressure extraction/ Subcritical water extraction (SWE)

Principles and mechanisms: Simple experimental equipment, the possibility of online coupling with other techniques, and the ability to use water as a solvent have boosted the number of utilization of Subcritical water extraction (SWE). Established at temperatures between 100°C

and 374°C (the critical temperature) under high pressure (usually from 1 to 6 MPa) water stays in the liquid state.

At the higher boundaries, extraction efficiency is obtained due to superior mass transfer properties of subcritical water. The variability of the dielectric constant with temperature is an important variable to consider (Carr et al., 2011). At room temperature the dielectric constant of water is close to 80. To obtain values of neighboring 27, such as ethanol at ambient temperature, water must be heated to 250°C.

The experimental apparatus required is fairly simple, consisting of a pressure pump, extraction pump, oven where the extraction takes place, valves to maintain a steady pressure in the system and a coolant to swiftly cool the obtained extract.

Subcritical fluid extraction of valuable bio-compounds from winery by-products: Several studies were conducted to compare SWE to traditional extraction methods, and numerous extraction parameters such as temperature, pressure, flow rate, sample mass were investigated and taken into consideration (Table 6). Optimal conditions for subcritical water extraction are in direct relation with various phenolic acids, anthocyanins and flavonoids. Temperature was the most influential factor in extraction yield and selectivity. With optimum extraction temperature dependent on the by products used and the targeted molecules. For the extraction of anthocyanins from dried red grape pomace, several temperatures ranging from 100 to 160°C were studied, SWE extracts at 110°C had higher levels of anthocyanins values than extracts obtained using conventional solvent extraction at 60% methanol (Zhi et al. 2005). While the extraction recovery of other families of compounds such as catechins and proanthocyanidins

from grape seeds showed that selective extractions of compounds can be realized using one-step extraction at 150°C (Garcia-Marino et al. 2006). The greater the temperature the better the extraction yield of gallic acid, while at lower temperatures thermolabile anthocyanins are extracted.

Adding a solvent to water during subcritical extraction leads to the acceleration of extraction and a higher recovery of anthocyanins from grape pomace that decreases the running cost of the extraction process. Optimum ranges for temperature and ethanol concentration are 100--120°C and 50--70% (v/v) respectively (Monrad et al., 2010). It should be mentioned however that the loss of some particular families of polyphenols (e.g. quercetins) has been reported when using only water as an extraction solvent. This is due to the fact that some polyphenols need more than half of methanol/ethanol to be efficiently extracted (Srinivas et al., 2011). This in turn, highlights the a relationship between the content of the organic solvent used and its selectivity to certain classes of compounds (Mustafa et al., 2011).

The main limit of this technology is the degradation of thermolabile compounds during extraction. At high temperature (250°C) during 30 minutes, the majority of flavonoids were degraded (Ko et al., 2014).

Stage of development, research needs and challenges:

In general, the use of SWE provides a number of advantages over traditional extraction methods since high diffusion rates promote very efficient extraction of the raw material. Furthermore, those rates vary according to different chemical structures of organic compounds. Therefore, extraction with subcritical water can be both selective and rapid. However SWE

extraction in a prolonged period could result in degradation. The development of brown, highly, odiferous compounds with high antioxidant capacity at high extraction temperatures suggested the participation of Maillard reactions in water (Rodríguez-Meizoso et al., 2008) and in ethanolic extracts (Howard & Pandjaitan, 2008).

Most studies have been performed in batch mode on a small scale, but continuous flow equipment has also been tested (Monrad et al., 2014). The feasibility of large-scale operations with energy estimation of subcritical water extraction has not been studied until now. A major drawback of this technology is the high operating pressure, which requires high initial investments compared to traditional methods extraction. Nevertheless the high purity of extracts and the efficiency of the process may lead to the future development on the industrial scale. Also, the possibility of fine-tuning the selectivity of polyphenol extraction through changes in water temperature, which directly varies the dielectric constant, is another advantage of subcritical water extraction (Ko et al., 2014).

3.2.2. Supercritical fluid extraction (SFE)

Principles and mechanisms: Above the critical point if a fluid is forced to a pressure and temperature, it becomes a supercritical fluid. Various properties of the fluid change under these conditions. The relatively low viscosity and high diffusivity (gas-like) values provide appreciable penetrating power into the matrix. Its relatively high (liquid-like) density gives good solvent power, generating higher rates of solute mass transfer into a supercritical fluid than into a liquid.

For apolar target molecules the main solvent used in SFE is carbon dioxide (CO₂), which has relatively low critical pressure of 7.4 MPa and a low critical temperature of 31.1°C (Sahena

et al., 2009). In addition CO₂ is safe, foodgrade and widely available with a relatively low cost and high purity (Díaz-Reinoso et al., 2006). The physicochemical properties of supercritical CO₂ facilitate mass transfer, yield to a solvent-free extract and allow an environmentally friendly operation. However, to use CO₂ as a solvent for polar analytes, a co-solvent such as ethanol is often added as a modifier to CO₂ (Wijngaard et al., 2012). Depending on the type of sample matrix and the affinity of the targeted compound for the matrix, ethanol may influence the extraction by increasing the solubility of the targeted compound in the supercritical CO₂ (SC-CO₂) as a result of compound--modifier interactions in the fluid phase. This is achieved by inducing the compound desorption from the matrix and/or by favoring the penetration of the SC-CO₂ into the matrix (Díaz-Reinoso et al., 2006).

Supercritical fluid extraction of valuable bio-compounds from winery by-products:

In by-products from wine processing, SC-CO₂ has been interestingly used for the recovery of polar bioactive compounds (Table 6). For instance, Bleve et al., (2008) developed SC-CO₂ for the purification of anthocyanins from grape skin extracts. The desired fraction containing pure anthocyanins with yields of 80--85%, compared to the initial extract, was obtained under the following optimized process conditions (10-13.10⁶ Pa, 30-40°C; pH 2-4; 25-30% of ethanol in the liquid matrix; CO₂ flow rate 25--50 mL/min).

Moreover, Casas et al., (2010) reported that resveratrol could be efficiently extracted using SC-CO₂ at high pressure (40 MPa) and low temperature (35°C) using 5% v/v ethanol as a co-solvent. SC-CO₂ extraction enabled resveratrol to be obtained from seeds, which was not possible by conventional methods. However, an increased ethanol concentration above 7.5%

caused a decrease in resveratrol recovery (Pascual-Martí, 2001). Mixture of ethanol-water was also investigated as co-solvent for biocompounds recovery from grape pomace (Da Porto et al., 2014). The highest extraction yields were obtained at 6 ml/min CO₂ and 10% of ethanol/water (57/43, v/v), which allowed the recoveries of 2.5 g of total polyphenols, 188 mg of monomeric procyanidins, 154 mg of oligomeric procyanidins and 361 mg of polymeric procyanidins /100 g dried material.

Stage of development, research needs and challenges:

Based on existing concepts, and noticeably for food and pharmaceutical products at industrial scale, the extraction of grape by-products by supercritical fluid should be feasible at larger scale (pilot and industrial scale). A study has calculated the economic feasibility of large-scale operations of supercritical fluid extraction (SFE) for the recovery of phenolics using grape by-products (Farías-Campomanes et al., 2013). An industrial SFE plant with a capacity of 0.5 m³ for producing an extract with an expected concentration of approximately 23 g of phenolic compounds /kg of dry byproduct, with an estimated manufacturing cost of US\$ 133 /kg.

Several studies stated that one of the biggest drawbacks is the high investment cost needed, in comparison to classical low-pressure equipment that is less costly. In addition, a more qualified manpower is required to operate the machinery. This is why SFE should be only considered for high added value products. Nevertheless, the high cost of investment needed may be overcome by increasing the volumes of extract being treated thus lowering the overall cost (Prado et al., 2012).

3.3. Comparison of extraction processes

Several studies performed at laboratory scale have aimed at comparing the extraction described above on the recovery of phenolic compounds from grape by-products, with no direct comparison between sub and supercritical extractions. The results evidenced that sub and supercritical extraction are more efficient for the recovery of total phenolic compounds. With high selectivity regarding the specific recovery for a family of compounds depending on the process used. Based on the previous observations, Table 7 resumes the advantages and drawbacks of the different extraction techniques.

4. Purification and fractionation of the extract

The large array of utilization of extracts in various fields has lead to further the search for multiple separation techniques of individual compounds. This field has not received much attention thus far, in particular concerning its application to large-scale, industrial purposes.

4.1. Solid phase extraction

Solid phase extraction (SPE) is a widely used technique in which the sample matrix passes through a column containing sorbent material (solid phase) on which the targeted compound is retained. Subsequently, with a correct choice of wash solvent the chosen compounds can be selectively removed, resulting in a highly purified extract (Sarker et al., 2005). The use of SPE for the separation of nonpolymeric from polymeric phenols was first proposed for red wine (Pinelo et al., 2006). Recently, SPE was used to specifically extract classes of phenolic compounds and organic acids from white grapes in one step (Dopico-García et al., 2007) which aimed at simplifying a solid-liquid extraction followed by a solid-phase extraction (SL-SPE)

method previously developed by the same group. In that approach, the authors used C18-based sorbents and concluded that matrix solid-phase dispersion (SL-SPE) was good for separation, especially for organic acids.

Additionally rapid solid-phase was proposed as an analysis, extraction and purification technique of resveratrol and other polyphenols in red wine (Hashim et al., 2013).

The isolation of dimeric to tetrameric procyanidins is achieved after removing the polymeric compounds by solvent precipitation. Purification on polyamide improved the purities of the B-type dimers isolated compounds (Köhler et al., 2008).

A complementary study proposed normal phase (NP) HPLC followed by reversed-phase (RP) HPLC as purification technique of B-type dimers. The yield for B1--4 from the grape seed extract using NP/RP-HPLC was about 10 times higher compared to the previously mentioned (Appeldoorn et al., 2009).

The uses of these purification methods have so far been restricted to analytical purposes only, due to the fact that preparative scale-up would be too expensive (given the cost of the stationary phases) at the industrial level.

4.2. Resin adsorption

Similar to solid phase separation, polyphenols in resin adsorption are retained by micro-beads and then specifically eluted using a wash solvent. With its relatively simple design, ease of regeneration, low cost of operation and scale up, resin adsorption appears as the most relevant technique for selective polyphenols recovery from liquid extracts (Soto et al., 2011).

Polyphenolic compounds are commercially purified and fractionated by resins adsorption, with recent developments in the field currently under consideration (Fu et al., 2005; Kammerer, et al., 2005; Schieber et al., 2003; Xia et al., 2012; Yang et al., 1997; Zhao et al., 2008). The resin used for the adsorption of lipophilic compounds, are lightly hydrophilic acrylic or nonpolar styrene--divinylbenzene resins which can then be washed and eluted with alcohols. Purification of individual compounds or compound classes are done by adjustment of process parameters that included flow rate, concentration of the solute pH value and temperature. Shrikhande et al., 2003 in their patent have proposed copolymer of trimethylolpropane trimethacrylate as an adsorbent resin to maximize the concentration and purification of the beneficial polyphenolic substances from grape seed extract. On a laboratory scale using a styrene--divinylbenzene copolymerisate resin for adsorption of anthocyanins from grape pomace for their purification and concentration. Noticably, by varying elution solvent selective results where obtained, with acidified methanol giving the optima results, recovery rates ranged from 96 to 100% of anthocyanins of the content. Scaling up from laboratory to pilot plant did not affect recovery rates (Kammerer et al., 2005). This field is fairly new and studies are required to characterize further resin adsorbents with regard to their potential to recover and fractionate phenolic compounds extracted. While this technique has its advantages it usually leads to highly concentrated fractions in organic solvents, and a further step of solvent elimination should be considered.

5.4. Membrane processes

Employing membranes having different structure and pore sizes it is possible to process and achieve good recovery of polyphenols from grape wastes, while at the same time, fractionating different chemical classes, according to their molecular masses (Crespo &

Brazinha, 2010). This process has the clear advantage of being of low environmental impact, as it utilizes little amounts of solvents, mild temperatures and low pressures.

Several studies have used membrane filtration as a concentration step. Accordingly, microfiltration (0.22 and 0.45 μm) of the aqueous EtOH extract from grape seeds purified the polyphenols in the final recovery (Nawaz et al., 2006): this method turned out to be low-cost, efficient and environmental friendly. More recently, grape seed extracts obtained with HVED were concentrated using membranes with different molecular weight cut off (0.15 μm , 150 and 50 kDa). Using 150 kDa and 50 kDa membranes, polyphenols were concentrated 2.2 and 2.5 times, respectively, as compared to the initial extract (Liu et al., 2011). Aqueous extracts from pressed distilled grape pomace were processed using ultrafiltration (1 kDa) and nanofiltration (250 Da, 300 Da, 350 Da) membranes to obtain enriched extracts. The 250 Da membrane allowed the concentration of total phenolic compounds up to 6.3 times the initial extract concentration (Díaz-Reinoso et al., 2009). Another aspect is the use of membrane processing to purify and fractionate extracts from winery wastes with the aim of obtaining proanthocyanic fractions with different degrees of polymerization, using different successive cut-off membranes molecules could be separated. Few studies have been conducted on this subject, and literature concerning it is very scarce, making it an advantageous topic for future studies.

5. Conclusion

The recovery of high added value compounds from winemaking byproducts is rapidly developing. The key to a successful extraction and purification is the identification of effective methods that could lead to extracts that meet consumers' high quality standards. Several of the

emerging technologies presented above such as subcritical water extraction and the purification by membranes processes have showed their effectiveness. However as presented in this review, the scale-up of these techniques, is not as simple in practice as it is on paper, in regards to affecting the functional properties of the targeted compounds.

Following the above consideration, restrictions in yield, and energy balance should also be further studied. For the pretreatment process, PEF and HVED technologies have shown their efficiency with low consumption of energy compared to other techniques. Further investigations are required to compare the energy utilized in different extraction and purification technologies. Finally, the extract produced is in a liquid form should transformed to a solid since it is the only marketable or with industrial interest form. This final stage utilizes important amounts of energy and is a very important stage to further evaluate.

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Table 1: Efficiency and operating conditions of PEF-assisted extraction used to extract bioactive compounds from grape by-products

Grape by-product matrix	Operating conditions	Extraction conditions	Targeted bio-compounds	Reference
			(Relative increase)	
Red grape pomace	30 exponential pulses in water	1h at 70°C in ethanol/water (50:50, v/v)	Anthocyanins (1.17) *	(Corrales et al., 2008)
(Dornfelder)	3 kV/cm, 10 kJ/kg		Polyphenols (1.59) *	
	Total treatment time: 15 sec			
White grape skins	100 bipolar pulses of rectangular shape without addition of conductive liquid	3h at 20°C in water	Polyphenols (1.12) *	(Boussetta et al., 2009a)
(Chardonnay)	1.3 kV/cm, 30 kJ/kg			

	Effective treatment time: 100 ms at 20°C			
Grape seeds	600 exponential pulses in water (L/S ratio: 5)	1h at 50°C in ethanol/water (30:70, v/v)	Polyphenols (1.30) *	(Boussetta et al., 2012a)
(Pinot Meunier)	20 kV/cm, 320 kJ/kg		Reduction of diffusion time by 2	
	Effective treatment time: 6 ms at 50°C			
Fermented grape pomace	1700 monopolar pulses of rectangular shape without addition of conductive liquid	7h at 20°C in ethanol/water (50:50, v/v)	Anthocyanins (1.19) *	(Brianceau et al., 2014)
(Dunkelfelder)	1.2 kV/cm, 18 kJ/kg		Polyphenols (1.13) *	
	Effective treatment time: 170 ms at 20°C			

Vine shoots	1500 exponential pulses in water (L/S ratio: 20)	4h at 50°C in	Polyphenols (2.09) *	(Rajha et al., 2014)
(Grenache blanc)	13.0 kV/cm, 762 kJ/kg	0.1 M of NaOH in water	Kaempferol: 0.156 mg/g	
	Effective treatment time: 15 ms at 50°C		Epicatechin: 1.747 mg/g	
			Resveratrol: 0.032 mg/g	
Fermented grape pomace	750 exponential pulses in water (L/S ratio: 10)	Without diffusion	Anthocyanins (5.3)**	(Barba et al., 2015)
(Dunkelfelder)	13.0 kV/cm, 272 kJ/kg		Polyphenols (0.47)**	
	Effective treatment time: 7,5 ms at 25°C			

* *In comparison with control extraction, performed in the same conditions but without PEF pre-treatment*

*** In comparison with control extraction of grinded pomace in water (2h -- 20°C under stirring)*

Table 2: Efficiency and operating conditions of HVED-assisted extraction used to extract bioactive compounds from grape by-products

Grape by-product matrix	Operating conditions	Extraction conditions	Targeted bio-compounds (Relative increase)	Reference
Unfermented red grape pomace (Chardonnay)	80 discharges in water (L/S ratio: 3) 40 kV -- 0.5 Hz 32 kJ/kg Effective treatment time: 0.8 ms at 60°C Laboratory scale -- in batch	1h at 60°C in water	Polyphenols (2.5) *	(Boussetta et al., 2009a)
White grape skins	60 discharges in water	3h at 20°C in water	Increase of initial soluble matter extraction by 7.5	(Boussetta, et al., 2009a)

(Chardonnay)	L/S ratio: 6 40 kV -- 0.5 Hz 120 kJ/kg 0.6 ms at 20°C Laboratory scale -- in batch		Polyphenols (1.2) *	
Unfermented red grape pomace (Pinot meunier)	150 discharges in water L/S ratio: 5 40 kV -- 0.5 Hz 80 kJ/kg Effective treatment time: 1.5 ms at 20°C Laboratory scale -- in batch	1h at 20°C in ethanol/water (30:70, w/w)	Polyphenols (11.1) *	(Boussetta et al., 2012b)
Unfermented grape skins (Pinot)	750 discharges in water	Without diffusion	Polyphenols (14) **	(Boussetta et al., 2012b)

Meunier and Chardonnay)	L/S ratio: 5 40 kV 400 kJ/kg Pilot scale -- in batch			
Grape seeds (Pinot Meunier and Chardonnay)	750 discharges in water L/S ratio: 5 40 kV 400 kJ/kg Pilot scale -- in batch	Without diffusion	Polyphenols (50) **	(Boussetta et al., 2012b)
Grape stems (Pinot Meunier and Chardonnay)	750 discharges in water L/S ratio: 5 40 kV 400 kJ/kg Pilot scale -- in batch	Without diffusion	Polyphenols (4) **	(Boussetta et al., 2012)

Grape seeds	100 discharges in water (L/S ratio: 5)		Polyphenols (1.5) *	
(Pinot meunier)	40 kV -- 0.5 Hz 53 kJ/kg effective treatment time: 1 ms at 50°C Laboratory scale -- in batch	1h at 50°C in ethanol/water (30:70, w/w)	Reduction of diffusion time by 4.6	<u>Boussetta et al. 2012a</u>
Vine shoots	500 discharges in water (L/S ratio: 20)	4h at 50°C in	Polyphenols (3.1) *	
(Grenache blanc)	40 kV -- 0.5 Hz 254 kJ/kg	0.1 M of NaOH in water	Kaempferol: 0.213 mg/g (not detected in untreated sample) Epicatechin: 2.459 mg/g	(Rajha, et al., 2014)

	effective treatment time: 5 ms at 50°C		(n.d. in untreated sample)	
	Laboratory scale -- in batch		Resveratrol: 0.414 mg/g	
			(n.d. in untreated sample)	
Fermented grape pomace	120 discharges in water (L/S ratio: 10)		Anthocyanins (3.4) ***	
(Dunkelfelder)	40 kV -- 0.5 Hz		Polyphenols (0.88) ***	
	44 kJ/kg	Without diffusion		(Barba et al., 2015)
	Effective treatment time: 1.2 ms at 25°C			
	Laboratory scale -- in batch			

Grape stems (Cabernet Franc)	400 discharges in acidified water (pH 2.5, L/S ratio: 7.5)	2h at 20°C in ethanol/water (50:50, v/v)	Polyphenols (1.4) *	(Brianceau et al., 2015)
	40 kV -- 0.5 Hz	pH 2.5	Flavan-3-ols (1.4) *	
	190 kJ/kg		Flavonols (1.2) *	
	Effective treatment time: 4 ms at 20°C		Stilbenes (1.2) *	
	Laboratory scale -- in batch			

* *In comparison with control extraction, performed in the same extraction conditions but without
HVED pre-treatment*

** *In comparison with 10 minutes of aqueous diffusion*

*** *In comparison with control extraction of grinded pomace in water (2h -- 20°C under
stirring)*

Table 3: Efficiency and operating conditions of US-assisted extraction used to extract bioactive compounds from grape by-products

Grape by-product matrix	Operating/extraction conditions	Targeted bio-compounds (Relative increase*)	Reference
Red grape pomace (Dornfelder)	<p>Ultrasonic bath -- 35 kHz</p> <p>V = 90 mL - 140 W</p> <p>60 min at 70°C</p> <p>≈ 4860 kJ/kg</p> <p>Ethanol/water (50:50, v/v) (L/S ratio = 4.5 (v/w))</p> <p>Laboratory scale -- in batch</p>	<p>Anthocyanins (0.98) *</p> <p>Polyphenols (1.68) *</p> <p>Antioxidant capacity (1.65) *</p>	(Corrales et al., 2008)
Grape seeds	<p>Ultrasonic bath -- 40 kHz,</p> <p>V = 100mL - 250 W</p> <p>29 min at 55-60°C</p> <p>≈ 4580 kJ/kg</p>	<p>Polyphenols:</p> <p>5.44 mg/100 mL</p>	(Ghafoor et al., 2009)

	Ethanol/water (53:47, v/v) (L/S ratio = 50 (v/w))		
	Laboratory scale -- in batch		
Dried Grape skins (Campbell Early)	<p>Ultrasonic bath -- 40 kHz</p> <p>V = 100mL - 250 W</p> <p>25 min at 45°C</p> <p>≈ 4032 kJ/kg</p> <p>Ethanol/water (52:48, v/v) (L/S ratio = 50 (v/w))</p> <p>Laboratory scale -- in batch</p>	<p>Anthocyanins: 6.26 mg/mL</p>	<p>(Ghafoor et al., 2011)</p>
Vine shoots (Pedro Ximenez)	<p>Titanium ultrasound probe</p> <p>14W/mL, (V = 20mL - 280 W)</p> <p>≈ 6930 kJ/kg</p> <p>7.5 min extraction at room temperature</p> <p>80% (v/v) aqueous ethanol at pH 3</p> <p>(L/S ratio = 20 (v/w))</p>	<p>Polyphenols: 546.4 µg/mL</p>	<p>(Delgado-Torre et al., 2012)</p>

	Laboratory scale -- in batch		
Red grape pomace	Titanium ultrasound probe, 55 kHz	Polyphenols: 770.9±77.5 mg /100 g dry weight (1.62)	
Syrah	0.44 W/mL (V = 200mL - 87 W) 60 min at 50°C ≈ 1490 kJ/kg Water (L/S ratio = 20 (v/w)) Laboratory scale -- in batch	Antioxidant capacity (ABTS): 705.9±41.7 mg TE/100g	(González-Centeno, et al., 2015)
Red grape pomace	Titanium ultrasound probe, 40 kHz,	Polyphenols: 2.31 mg GA/100 g fresh weight (fw)	
Syrah	0.15 W/mL (V traité = 1 L - 150 W)	Flavonols: 2.04 mg quercetin/100 g fw	(Reyes González-Centeno et al., 2014)

	<p>≈ 187.5 kJ/kg</p> <p>Water (L/S ratio = 5 (v/w))</p> <p>25 min at 17°C</p> <p>Laboratory scale -- in batch</p>		
Vine shoots	Titanium ultrasound probe, 24 kHz	Polyphenols (1.45)	
(Grenache blanc)	<p>1.3 W/mL (V traité = 300 mL - 400 W)</p> <p>≈ 3428 kJ/kg</p> <p>45 min at 50°C in water - (L/S ratio = 20 (v/w))</p> <p>+ Subsequent solid-to-liquid diffusion: 4h at 50°C in 0.1 M of NaOH in water</p> <p>Laboratory scale -- in batch</p>	<p>Kaempferol: 0.097 mg/g</p> <p>Epicatechin: 0.671 mg/g</p> <p>Resveratrol: 0.024 mg/g</p>	(Rajha, et al., 2014)
Fermented grape pomace	Titanium ultrasound probe, 24 kHz	Anthocyanins (4.3)**	(Barba et al., 2015)

(Dunkelfelder)	1 W/mL (V traité = 400 mL - 400 W) ≈ 1527 kJ/kg 28 min at 25°C in water (L/S ratio = 10 (v/w)) - Laboratory scale -- in batch	Polyphenols (0.44)**
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- *In comparison with control extraction, performed in the same extraction conditions but without US treatment*
 - *** In comparison with control extraction of grinded pomace in water (2h -- 20°C under stirring)*

Table 4: Advantages and drawbacks of traditional and alternative pre-treatment techniques

	Drying/Grinding	PEF assisted extraction	HVED assisted extraction	US assisted extraction
Advantages	<p>Easy implementation</p> <p>- High extraction efficiency</p>	<p>- Low energy requirements</p> <p>- Low processing costs</p> <p>- High selectivity, particularly for anthocyanins</p>	<p>- Low energy requirements</p> <p>- High extraction efficiency</p>	<p>Easy implementation</p> <p>Easy-operating</p> <p>High extraction efficiency</p> <p>- High adaptability of the US devices to the different raw material</p>
Drawbacks	<p>- Overheating of the plant matrix</p>	<p>- Poor adaptability of the PEF apparatuses (generator & treatment cells) to the different raw</p>	<p>- Possible degradation of bio-compounds</p>	<p>- Possible degradation of bio-compounds</p>

		material		
	- Possible degradation of the bio-components	- High investment cost	- Treatment in batch	- Erosion of the transducers
	- High energy consumption		- Limited lifetime of electrodes	
	- Increased difficulties during the filtration and purification steps		- Increased difficulties during the filtration and purification steps	
	- Poor selectivity		- Poor selectivity	

Table 5: Comparison of literature works on optimization of solvent extraction of phenolic constituents from grape by-products (adapted from (Spigno et al., 2007))

Grape by-product matrix	Variables	Targeted bio-compounds	Reference
Fresh seeds from white grape pomace (Riesling)	Binary mixtures of ethyl acetate and water (from 3.3 to 20% of water) Extraction time (from 1 to 24h)	Proanthocyanidins	(Pekić et al., 1998)
Dried powdered defatted seeds from fresh red grape (Bangalore blue)	Solvent: acetone, ethyl acetate, methanol and binary mixtures of ethyl acetate and water (from 10 to 20% of water)	Flavan-3-ols Antioxidant capacity	(Jayaprakasha et al., 2001)
Red grape pomace	Solvent: ethanol, methanol, water	Polyphenols	(Pinelo et al., 2005b)

(Grenache)	<p>Liquid-to-solid ratio (from 1 to 5 (v/w))</p> <p>Extraction time (from 30 to 90 min)</p> <p>Temperature (from 25 to 50°C)</p>	Antioxidant capacity	
Red grape pomace	<p>In a continuous process: Solvent flow rate: (from 2 to 3 ml/min)</p>	Polyphenols	
(Grenache)	<p>Sample amount (from 2.5 to 7.5 g)</p> <p>Particle size (from 0.5 to 5.5 mm)</p>	Antioxidant capacity	(Pinelo et al., 2005)
Fermented grape pomace	<p>Solvent: Water, 70% ethanol in water, 70% methanol in water</p>	Polyphenols	(Lapornik et al., 2005)

(Pinot noir)	Extraction time (from 1h to 24h)	Antocyanins	
		Antioxidant capacity	
Seeds and skins from white (Chardonnay) and red (Merlot) vinifications	Binary mixtures of water and ethanol or methanol or acetone	Polyphenols	(Yilmaz & Toledo, 2006)
		Antioxidant capacity	
Grape pomace	Temperature (from 28°C to 60°C)		
(Barbera)	Maceration times (from 1h to 24h)	Total phenolic compounds, tannins, anthocyanins, Cinnamic acids and flavonols	(Spigno et al., 2007)
	% of ethanol in water (from 10 to 60%)		
Dried grape skins from white grape pomace	Particle size (from 0.16 more than 0.63 mm)		(Bucić-Kojić, Planinić, Tomas, Bilić, & Velić, 2007)
	Liquid-to-solid ratio (from 10 to 40)	Polyphenols	

	Temperature (from 25 to 80°C)		
Fresh seeds and skins from white grape pomace (Roditis)	Binary mixtures of water and ethanol (from 28.5 to 57%) pH	Polyphenols Flavonoids Flavanols Proanthocyanidins Antioxidant capacity	(Makris et al., 2007)
Dried and milled fermented grape pomaces (Refošk, Merlot and Cabernet)	Binary mixtures of water and ethanol or ethyl acetate or acetone (from 50 to 100%) pH (from 2 to 6) Temperature (from 20 to 60°C)	Polyphenols Anthocyanins Quercetin Flavanols	(Vatai et al., 2009)

		Resveratrol	
Dried, milled and deffated grape stems	pH (from 2 to 6)	Polyphenols	
(Agiorgitiko, Moschofilero, Savatiano)	Binary mixtures of water and ethanol (from 40 to 60%)	Proanthocyanidins	(Karvela et al., 2009)
	Extraction time (from 1 to 5h)	Flavones	
		Flavanols	
Dried seeds, skin and pomace	Binary mixtures of water and ethanol or methanol or acetone (50/50, v:v)	Polyphenols	
(Pinot noir and Pinot meunier)		Flavonols, Flavanols	(Cheng et al., 2012)
		Anthocyanins	
		Antioxidant capacity	
Dried grape pomace	Solvent: Water, Ethanol/water (60/40, w:w)	Polyphenols	(Brazinha et al., 2014)

(Tempranillo)	Effect of citric acid (3 g/L) in the solvent	Gallic acid, catechin, epicatechin, resveratrol	
		Antioxidant capacity	

Table 6: Efficiency and operating conditions of SWE-assisted extraction used to extract bioactive compounds from grape by-products

Grape by-product matrix	Operating/extraction conditions	Targeted bio-compounds (Relative increase*)	Reference
Red grape pomace (A-1575)	10 MPa, 110°C, 100% water, 1400 µg/mL sodium metabisulfite	Total polyphenols: 6.23 g/100g Total anthocyanins: 5.93 mg/100g Anthocyanins, Flavonols, Hydroxycinnamates (1)	(Ju & Howard, 2003)
Grape seeds (Tempranillo)	6-7 MPa, 150°C, 100% water	Gallic acid: 232.1 mg/100 g (6.3)	(García-Marino, et al., 2006)
Red grape pomace	8 MPa, 120°C, 1:1 (v/v) ethanol, 0.8% (v/v) HCl	Total polyphenols: 12.6 mg/100 g (7)	(Luque-Rodríguez et al., 2007)

		Total flavanols: 3.5 mg/100 g (11.6)	
Red grape pomace	10 MPa, 150°C 100% water	Total polyphenols: 6.070g/100g Total flavonoid: 1.425g /100g	(Casazza, et al., 2010)
Grape skins (Sunbelt grapes)	6.8 MPa, 100°C 50% ethanol/water (v/v)	Anthocyanins: 450 mg/100 g (1)	(Monrad et al., 2010b)
Red grape pomace (Cortina)	11.6 MPa, 140°C; 100% water	Total polyphenols: 3.08 g/100 g	(Aliakbarian, et al., 2012)
White grape pomace (Zinfandel)	10 MPa, 140°C, 100% water	Anthocyanins 130 mg/100 g Procyanidin 2077 mg/100 g	(Monrad, et al., 2012)

Table 6: Efficiency and operating conditions of SFE-assisted extraction used to extract bioactive compounds from grape by-products

Grape by-product matrix	Operating/extraction conditions	Targeted bio-compounds (Relative increase*)	Reference
White grape seeds	30 MPa, 55°C, 20 min, 20% v/v methanol/water	Low molecular weight polyphenols (> 0.9)	(Murga, Ruiz, Beltrán, & Cabezas, 2000)
Grape skins	15 MPa, 40°C, 7.5% ethanol/water, time 15 min	Resveratrol (1.0)	(Pascual-Martí, 2001)
Distilled white grape pomace (Grenache blanc)	50°C, 90 min, 8% v/v ethanol, L/S 1:1	Gallic acid, catechin and epicatechin	(Pinelo, Ruiz-Rodríguez, et al., 2006)

<p>Liquid grape skins extract</p> <p>(Malvasia nera)</p>	<p>10--13 MPa, 30--40°C; pH 2--4; 25--30% v/v ethanol/water flow rate 25--50 mL/min</p>	<p>Purification of total anthocyanins (0.85)</p>	<p>(Bleve et al., 2008)</p>
<p>White grape pomace</p> <p>(Palomino fino)</p>	<p>40 MPa, 55°C, 5% v/v ethanol/water</p>	<p>Resveratrol: 19.2 mg/100 g (21.3)</p>	<p>(Casas et al., 2010)</p>
<p>Grape seeds</p> <p>(Palomino fino)</p>	<p>40 MPa, 55°C, 5% v/v ethanol/water</p>	<p>Resveratrol: 11.1 mg/100 g (not detectable after conventional extraction in methanol/HCl (0.1%))</p>	<p>(Casas et al., 2010)</p>
<p>Grape skins</p> <p>(Palomino)</p>	<p>40 MPa, 35°C, 5% v/v ethanol/water</p>	<p>Resveratrol: 49.1 mg/100 g (15.8)</p>	<p>(Casas et al., 2010)</p>

fino)			
Grape stems (Palomino fino)	40 MPa, 35°C, 5% v/v ethanol/water	Resveratrol: 0.9 mg/100 g (0.41)	(Casas et al., 2010)
Grape skins (Campbell Early)	1.56--1.6 MPa, 45--46°C, 6--7% v/v ethanol/water	Polyphenols: 2.156 mg/100 mL, Anthocyanins: 1.176 mg/mL.	(Kashif Ghafoor, Park, & Choi, 2010)
Red grape pomace (Uvina)	20 MPa, 40°C 10% v/v ethanol/water	Gallic acid (11.2), protocatechuic acid (7), vanillic acid (10.7), <i>p</i> -hydroxybenzoic acid (14.6), syringic acid (16.3), <i>p</i> -coumaric acid (8.8), quercetin (3.4)	(Farías-Campomanes et al., 2013)

Grape pomace	20 MPa, 40°C	Polyphenols (0.92), Monomeric flavan-3-ols (157)	(Da Porto, Decorti, et al., 2014)
	10% of v/v ethanol/water (57/43, v/v)	Oligomeric flavan-3-ols (38.5)	
		Polymeric flavan-3-ols (2.4)	

** In comparison with control extraction*

Table 7: Advantages and drawbacks of traditional and alternative extraction techniques

	Organic solvent extraction	SWE extraction	SFE extraction
Stage of development	Industrial	Laboratory & Pilot	Industrial
Advantages	<ul style="list-style-type: none"> -Easy - Low cost -Doesn't require special equipment and qualified personnel 	<ul style="list-style-type: none"> - Easy implementation - Easy-operating High extraction efficiency - No solvent used 	<ul style="list-style-type: none"> - Low energy requirements - High extraction efficiency
Drawbacks	<ul style="list-style-type: none"> - Time consuming 	<ul style="list-style-type: none"> - Possible degradation of bio-compounds at high temperatures 	<ul style="list-style-type: none"> - Require low quantities of solvent to be effective

	<ul style="list-style-type: none"> - Possible degradation of the bio-components - High energy consumption for solvent regeneration - Traces of solvent 	<ul style="list-style-type: none"> - Treatment in batch - High cost 	<ul style="list-style-type: none"> - Treatment in batch - Complex expensive - Require specially trained personnel - High Cost
Investment	Low	To be evaluated	High 100--200 k€ (0.05m ³)
Selectivity	Low	High	High

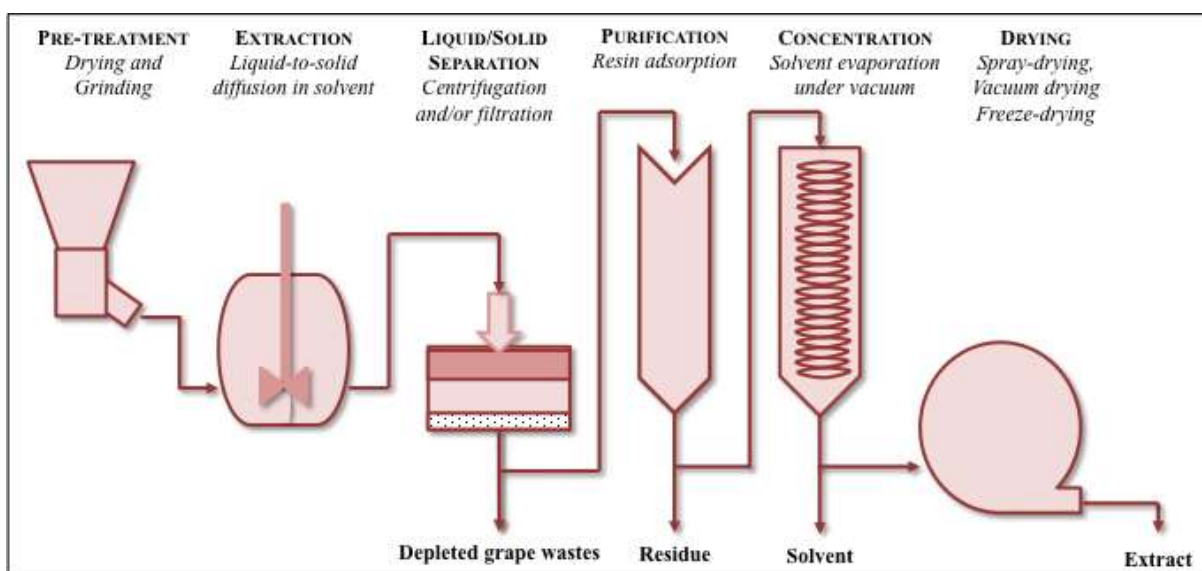


Figure 1: Conventional extraction procedure for the recovery of high added value components from grape wastes

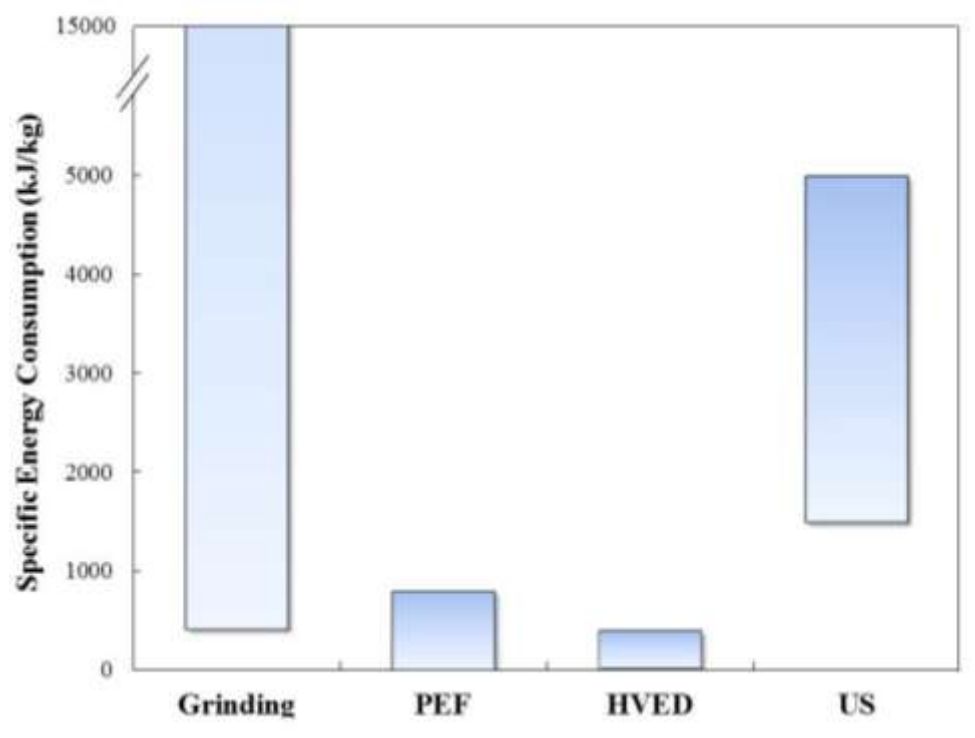


Figure 1: Comparison of specific energy consumption for the different pre-treatments of the raw material