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CHAPTER 3

Pressurized hot water extraction of polyphenols from plant material

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3.1 Introduction

The growing concern for human well-being has generated an increase in the demand for polyphenols, secondary plant metabolites that exhibit antioxidant, radical-scavenging, antibacterial, antiviral, enzyme-inhibiting, and antimutagenic properties (Serrano et al. 2009; Quideau et al. 2011). In fact, the demand for polyphenols (in terms of revenue) is expected to grow at a compound annual growth rate (CAGR) of 6.1% from 2012 to 2018, mainly due to the applications in functional foods and dietary supplements (Transparency Market Research 2013). Hence, polyphenols are useful plant-derived compounds for the food and pharmaceutical industries, which are focused in generating bioactive natural products for human health and nutrition.

Obtaining polyphenols from plant material for their application in the food and pharmaceutical industries involves the use of adequate extraction processes. Traditionally, the extraction of polyphenols (and phytochemicals in general) has been based mainly on the use of Soxhlet devices and organic solvents. The Soxhlet technique repeatedly brings fresh solvent into contact with the solid matrix, do not require a filtration procedure, and is simple to operate (Wang and Weller 2006). Nevertheless, traditional extraction methods such as Soxhlet employ large amounts of questionable solvents, are time-consuming and have low selectivity and/or low extraction yield (Ollanketo et al. 2002; Herrero et al. 2006a). Besides, extraction with organic solvents might generate unsafe and potentially hazardous products for human consumption and the environment. Therefore, the use of clean, innocuous, environmentally friendly, and efficient processes to extract polyphenols from plant material becomes appealing. Water-based extraction processes arise as a good option: Water is nonflammable, nontoxic, readily available, and an environmentally acceptable solvent. However, these processes are not widely used as an extraction method for plant

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materials because water is too polar to dissolve most organics, such as polyphenols (Ong et al. 2006). Indeed, given their nature and prevalence of nonionic bonds in their structures, most typical polyphenols present relatively low solubility in water at ambient conditions (Abou El Hassan et al. 2000; Boumendjel et al. 2003; Tommasini et al. 2004). Nonetheless, several physicochemical properties of water such as polarity, surface tension, viscosity, and dissociation constant can be manipulated through the change in temperature to improve the effectiveness of the extraction process (Hawthorne et al. 2002; King et al. 2010). Pressurized hot water extraction (PHWE, also called superheated water extraction, subcritical water extraction, pressurized low-polarity water extraction, hot compressed water extraction) process takes advantage of this feature, providing higher selectivities and shorter extraction times and avoiding the use of toxic organic solvents (King 2000). Thus, PHWE appears as an attractive alternative to common organic extraction methods for obtaining polyphenols from plant materials.

3.2 Polyphenols: Key bioactive compounds

Polyphenols can be defined as secondary metabolites of relatively high molecular weight and diverse structural complexity that are synthesized by plants exclusively from the shikimate-derived phenylpropanoid and/or the polyketide pathway(s) in response to different types of stress (hydric or saline) or aggressive factors (bacteria, fungi, virus, ultraviolet radiation, etc.) (Haslam 1998; Serrano et al. 2009; Quideau et al. 2011; Carrasco and Mizgier 2013). Polyphenols are widely distributed in the higher plant kingdom (Table 3.1); they are present in fruits, vegetables, herbs, spices, tea, and wine (Moure et al. 2001; Schieber et al. 2001; Djilas et al. 2009). They show a great diversity of structures, ranging from rather simple molecules to polymers (Manach et al. 2004), with or without glycosylation and/or esterification. They may be classified in different groups as a function of the number of phenol rings that they contain and the structural elements that bind one ring to another. Four main groups can be distinguished (Figure 3.1): (1) phenolic acids (hydroxybenzoic acids, hydroxycinnamic acids, hydroxyphenylacetic acids, hydroyphenylpropanoic acids and hydroxyphenylpentanoic acids); (2) flavonoids (anthocyanins, chalcones, dihydrochalcones, dihydroflavonols, flavanols, flavanones, flavones, flavonols, and isoflavonoids); (3) stilbenes, and (4) lignans and other polyphenols (alkylmethoxyphenols, alkylphenols, curcuminoids, furanocoumarins, hydroxybenzladehydes, hydroxybenzoketones, hydroxycinnamaldehydes, hydroxycoumarins, hydroxyphenylpropenes, methoxyphenols, naphtoquinones, tyrosols, phenolic terpenes, and others) (Neveu et al. 2010).

Polyphenols have the ability to complex strongly with metal ions and macromolecules such as polysaccharides and proteins (Haslam 1998); hence, they present biological activities that make them attractive for nutraceutical and

Table 3.1 Sources of polyphenols. Information was collected from Moure et al. (2001), Schieber et al. (2001), and Dimitrios (2006).

Source	Polyphenols
Fruits	
Berries	Flavanols hydroxycinammic acids, hydroxybenzoic acids, anthocyanins
Cherries	Hydroxycinnamicacids, anthocyanins
Blackgrapes	Anthocyanins, flavonols
Citrus fruits	Flavanones, flavonols, phenolic acids
Plums, prunes, apples, pears, kiwi	Hydroxycinnamic acids, catechins
Vegetables	
Aubergin	Anthocyanins, hydroxycinnamic acids
Chicory, artichoke	Hydroxycinnamic acids
Parsley	Flavones
Rhubarb	Anthocyanins
Sweet potato leaves	Flavonols, flavones,
Yellow onion, curly	Flavonols
Parsley	Flavones
Beans	Flavanols
Spinach	Flavonoids, *p*-coumaric acid
Cereals and teas	
Oats, wheat, rice	Caffeic and ferulic acids
Black and green tea	Flava-3-ols, flavonols
Herbs and spices	
Rosemary	Carnosic acid, carnosol, rosmarinic acid, rosmanol
Sage	Carnosol, Carnosic acid, lateolin, rosmanul, rosmarinic acid
Oregano	Rosmarinic acid, phenolic acids, flavonoids
Thyme	Thymol, carvacrol, flavonoids
Summer savory	Rosmarinic, carnosol, carvacrol, flavonoids
Ginger	Flavonoids and phenolic acids
By-products of fruit processing	
Apple pomace	Catechins, hydroxycinnamates, phloretin glycosides, quercetin glycosides, and procyanidins
Grape pomace	Anthocyanins, catechins, flavonol glycosides, phenolic acids and stilbenes
Citrus fruits pomace	Hesperidin, narirutin, naringin and eriocitrin
Mango seed	Gallic and ellagic acids, gallates, gallotannins and condensed tannin
Banana bracts	Anthocyanidins (delphinidin, cyanidin, pelargonidin, peonidin, petunidin and malvidin)
Kiwifruit pomace	Phenolic acids, flavanol monomers, dimers and oligomers, and flavonol glycosides
By-products of vegetable processing	
Onion residues	Quercetin glycosides
Olive residues	Hydroxytyrosol and derivatives

(*Continued*)

Table 3.1 (*Continued*)

Source	Polyphenols
Red beet pomace	p-coumaric and ferulic acids
Potato peels	Phenolic acids (chlorogenic, gallic, protocatechuic and caffeic acids)
Other by-products	
Durum wheat bran	Phenolic acids (chlorogenic, syringic, protocatechuic, gentisic, p-coumaric and vanillic acids)
Fraxinus ornus bark	Hydroxycoumarins
Corn bran hemicellulose	p-coumaric and ferulic acids
Oat hulls	Vanillic, p-coumaric and ferulic acids, catechol

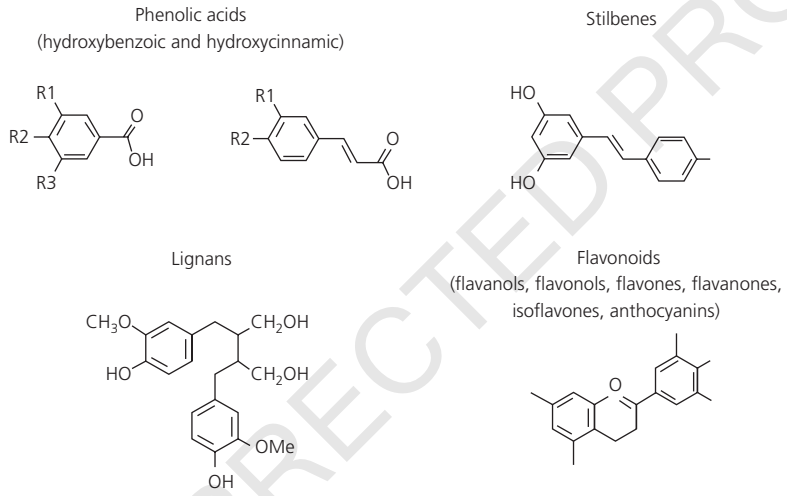

Figure 3.1 Main classes of polyphenols.

medicinal applications (Collins 2005; Manach et al. 2005; Scalbert et al. 2005; Ramassamy 2006; Hooper et al. 2008; Jensen et al. 2008). Particularly, polyphenols play a key role in the inhibition of enzymes related to cardiovascular and neurodegenerative diseases, as well as cancer and diabetes (Quideau et al. 2011). There is evidence that they prevent oxidation of LDL-lipoprotein (Frankel et al. 1993; Fuhrman et al. 1997; Landbo and Meyer 2001), platelet aggregation (Guerrero et al. 2007; Nardini et al. 2007), and oxidative cell damage (Spormann et al. 2008; Paiva-Martins et al. 2009). Additionally, polyphenols act as antimutagens, anticarcinogens (Kuroda and Hara 1999; Cardador-Martinez et al. 2002), and antimicrobial agents (Chung et al. 1998; Yoda et al. 2004). Moreover, phenolic acids and flavonoids are the focus of recent studies because of their antioxidant properties, which are stronger than those of other commonly used natural and synthetic antioxidants (Chen and Ho 1997; Miura et al. 2002).

Despite their demonstrated bioactive properties, the action of polyphenols on biological systems is complex and disputed because it is affected by bioavailability, doses, metabolism, and other biotransformations. Bioavailability is strictly related to their structures, like degree of glycosylation and conjugation with other polyphenols. For example, polymers such as proanthocyanidins may have direct effects on the stomach (Pastene et al. 2009) and intestinal mucosa, protecting these tissues from oxidative stress or carcinogen action (Manach et al. 2005). In addition, non-glycosylated phenolic compounds may be absorbed directly into the small intestine (Manach et al. 2004). In turn, to become absorbed in the intestine, polyphenols present in the form of esters, glycosides, or polymers require hydrolyzation by enterocyte enzymes or through the action of colonic microbiote (Carrasco and Mizgier 2013).

The antioxidant activity of polyphenols is arguable. On the one hand, studies in cell line cultures have shown that polyphenols are able to reduce oxidative stress and activate the antioxidant response of the cells. On the other hand, they could decrease cell viability and proliferation and induce cell apoptosis by acting as prooxidants and generating free radicals (Xia et al. 2010). The effects of polyphenols in cell cultures (either protective antioxidant or prooxidant/cytotoxic) will depend on several factors such as their concentration, their ability to oxidize, their lipophilicity, the content of other antioxidants and metals, and the oxidative stress level of the cell culture (Wei et al. 1995; Sergediene et al. 1999; Surh et al. 1999; Hou et al. 2004; Fujii et al. 2006; Halliwell 2008). Therefore, to safely use polyphenols as bioactive compounds it is necessary to carefully study aspects such as the specific dose, the delivery vehicle, the nutritional and health history, and the characteristics of the microbiota of the target population (Manach et al. 2004).

3.3 Pressurized hot water extraction process

Several physicochemical properties of water such as polarity, surface tension, viscosity, diffusivity, and dissociation constant can be manipulated by changing its temperature. For instance, water polarity is dramatically reduced while increasing temperature due to the breakdown of the hydrogen bonds that form the water structure. The dielectric constant (ε, measure of polarity) of water at 25°C is approximately 80 (extremely polar), but at 250°C, the water in liquid state reaches values of ε between 25 and 27, which are comparable to the values of methanol (ε=33) and ethanol (ε=24) at 25°C (Ong et al. 2006; Teo et al. 2010). Also, the viscosity and surface tension of water decrease with the temperature (Hawthorne et al. 2002) (Figure 3.2). On the contrary, high temperatures increase the diffusivity and dissociation constant of water (Holz et al. 2000; Bandura and Lvov 2006).

PHWE takes advantage of the features described before by raising the temperature to values within 100°C and 374°C, while applying sufficient pressure to

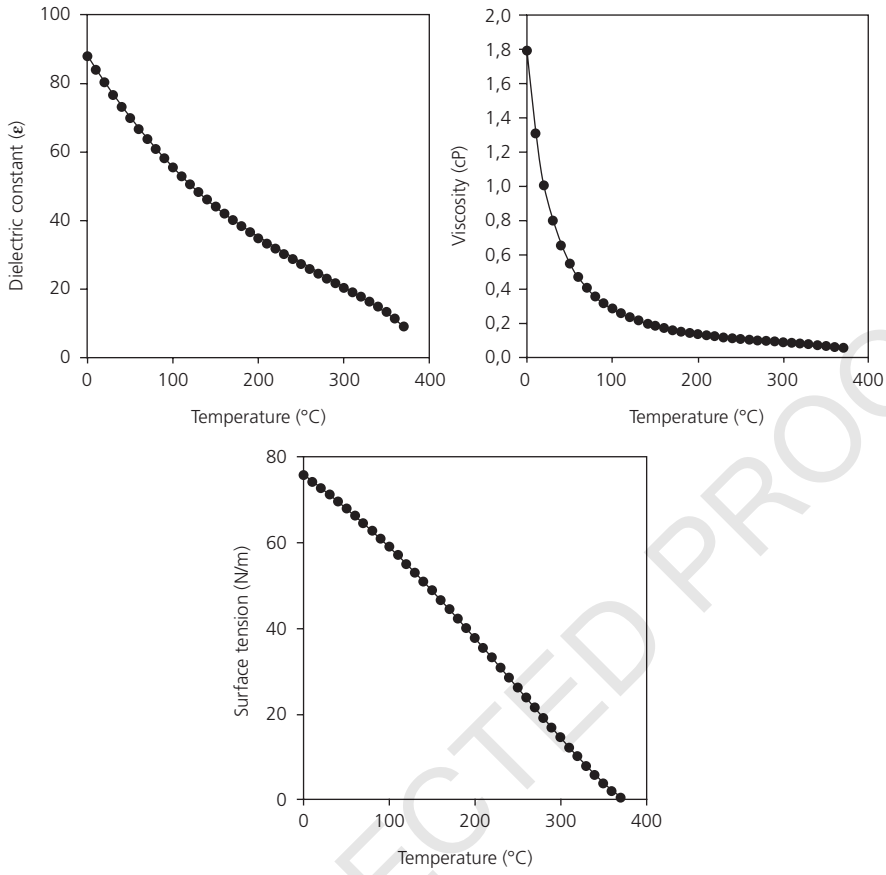

Figure 3.2 Decrease of the dielectric constant, viscosity, and surface tension of water with temperature. Data obtained from Beaton (1987).

maintain water in the liquid state. Both temperature and pressure play a significant role in the disruption of surface equilibrium decreasing the activation energy required for the desorption process (Hawthorne et al. 2002; Clifford 2005; Ong et al. 2006; Smith 2006). Besides, the ~~increases~~ in viscosity and surface tension of water enhance solvent penetration and wetting of the matrix (Teo et al. 2010). Higher diffusivities favor mass-transfer rates by disrupting intermolecular forces (i.e., van der Waals forces, hydrogen bonds, and dipole attractions) (Herrero et al. 2013). Moreover, changes in the dissociation constant of water facilitate the release of interest compounds from vegetable matrices since pressurized hot water act as an acid and/or base catalyst for reactions, such as hydrolysis of lignocellulosic material (Yu et al. 2007). Despite all the advantages of PHWE, the target compounds may also be subjected to thermal decomposition and hydrolytic attack (Ju and Howard 2005; Vergara-Salinas et al. 2012, 2013).

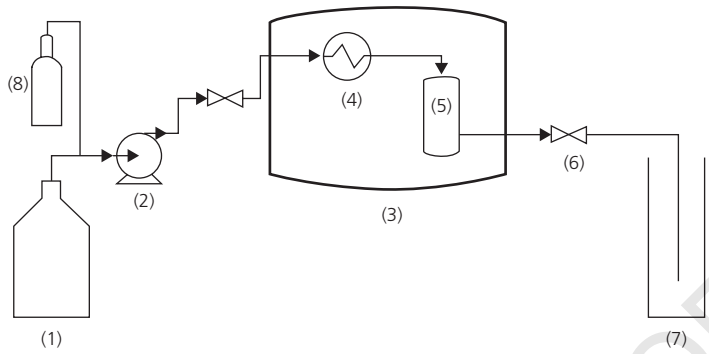

Figure 3.3 Typical system for PHWE processes. It consists of (1) a water container; (2) a water pump; (3) an oven; (4) a preheating coil; (5) an extraction cell; (6) a restrictor or valve; (7) a trapping vial; and (8) a modifier pump or N2 container (optional). Adapted from Herrero et al. (2013).

Typically, PHWE processes are carried out in a system such as that shown in Figure 3.3. In this system, the extraction cell containing the sample (e.g., the plant matrix) is filled with water, heated to the desired temperature and pressurized to maintain water as a liquid; then the extraction occurs (Raynie 2006). A pump is used to pressurize and transport water from a container, a preheating coil brings the water up to the operating temperature before entering into the extraction cell, an oven maintains the temperature in the extraction cell, a valve or restrictor is used to generate the required back pressure, and a trapping vial collects the extract. Optionally, the system can include a nitrogen circuit to purge the cell after the extraction and a coil to cool the water exiting the oven (Teo et al. 2010; Herrero et al. 2013). The extraction process is performed at pressures between 10 and 60 bar (typically 50 bar) and temperatures above the boiling point of water (up to 200–250°C).

The extraction mechanism of PHWE involves four sequential steps: (1) desorption of solutes from the matrix; (2) diffusion of the extraction fluid into the matrix; (3) partition of the solutes from the matrix into the extraction fluid; and (4) chromatographic elution of the solutes from the extraction cell to the collection vessel. Therefore, the process may be controlled by several phenomena such as solubility, sorption equilibria, and diffusion, whose incidence depends on the extraction modes and conditions (Teo et al. 2010; Mustafa and Turner 2011). The extraction can be performed in static or dynamic mode. In static mode, the most frequently used, the raw plant material is kept in the extraction cell with a given volume of water during a certain period of time at fixed conditions of pressure and temperature. Therefore, the extraction time and cycles of extraction (replacement of the solvent to deplete the matrix) must be carefully optimized. The extraction time must

allow the saturation of water with the target compounds and minimize the exposure of the compounds to high temperature. Generally, in static PHWE, the equilibrium is quickly reached (5–30 minutes) (Mukhopadhyay and Panja 2010).

In dynamic extraction mode, the pressurized hot water passes continuously through the matrix kept in the extraction cell (it can be called a semi-continuous process). The phase equilibria might be displaced and the efficiency of the extraction process might be increased (Herrero et al. 2013). Besides extraction time, the water flow rate (usually within the range of 1–1.5 mL/min) is another important optimization parameter of PHWE operating in dynamic mode (Teo et al. 2010). If the flow rate is large enough, the diffusion of the solute within the matrix (internal mass transfer) controls the process, and therefore further increase in the flow rate would have little effect on the extraction rate (Pronyk and Mazza 2009). If the flow rate is too low, the removal of the solute from the surface of the matrix decreases, and the extraction is controlled by external mass transfer from solid to the solvent. In this case, an increase in the flow rate would result in an increase of the extraction rate of the solute (Pronyk and Mazza 2009). Despite its advantages, dynamic PHWE generates more diluted extracts than those obtained in static mode, increasing posttreatment costs (Herrero et al. 2013).

PHWE has the advantages of being relatively inexpensive, minimizes or totally avoids the use of objectionable solvents, and provides a facile means for supplying a wide spectrum of concentrated phytochemicals for food formulation, dietary supplements, and phyto-pharmaceutical applications (King and Grabiel 2007). Thus, several review articles (Smith 2002; Herrero et al. 2006a; Ong et al. 2006; Mendiola et al. 2007; Wiboonsirikul and Adachi 2008; Mukhopadhyay and Panja 2010; Teo et al. 2010; Mustafa and Turner 2011; Herrero et al. 2013), book sections (Clifford 2005; Cacace and Mazza 2006a; Srinivas and King 2010), and patents (Hawthorne et al. 2002; King and Grabiel 2007) that cover or are completely dedicated to the PHWE of phytochemicals have been published. Even, articles about design, performance improvements, and scaling-up of the extraction process of bioactive compounds at high temperature and pressure (Ibañez et al. 2009; King and Srinivas 2009; Pronyk and Mazza 2009; Srinivas et al. 2009; Monrad et al. 2012; Rodríguez-Meizoso et al. 2012) have been published recently, demonstrating the increasing interest in the development of these green extraction processes. Additionally, pressurized hot water has been used for other applications such as selective separation of organic compounds from liquids, selective separation of organic compounds using adsorbent phases, improvement of reactions controlling the dissociation constant, and cleaning of waste water and oxidative degradation compounds for soil remediation (Yang et al. 1995; Hawthorne et al. 2000; Fields et al. 2001; Kuosmanen et al. 2002; Yesodharan 2002; Coym and Dorsey 2004; Ong et al. 2006; Soltanali et al. 2009).

3.4 Pressurized hot water extraction to isolate plant polyphenols

In this section, the key parameters for designing and optimizing the PHWE processes of polyphenols (e.g., aqueous solubility and temperature) and their effects on extraction yields and extracts activity and composition are analyzed. Also, operation modes and equipment for the PHWE of polyphenols are described. Finally, the application of PHWE to obtain different polyphenols from plant sources is discussed and compared with traditional solvent extraction methods.

3.4.1 Solubility of polyphenols in pressurized hot water

Aqueous solubility is a key parameter for designing and optimizing PHWE processes. Particularly, aqueous solubility controls the first stage of the PHWE process, where the external mass transfer occurs. In this stage, the solute (mainly present on the surface of the material being processed) is freely available to be removed as long as the maximum solubility of the solute within the solvent (in our case, water) has not been reached (Pronyk and Mazza 2009).

High pressures used in PHWE have practically no effect on the aqueous solubility, since water in those conditions (as well as other liquids in subcritical conditions) is largely incompressible (Smith 2002). Solubility in pressurized hot water is primarily regulated by temperature, which weakens the intermolecular hydrogen bonds within water and reduces its dielectric constant (and therefore its polarity). At ambient conditions, the dielectric constant of water is 80 and it can reach a value of 27 at 5 MPa and 250°C (Yang et al. 1995), which is close to those of organic solvents such as ethanol and methanol at 25°C. Hence, water becomes a solvent suitable to dissolve many hydrophobic compounds (aqueous solubility increases) as temperature increases above 100°C (at adequate high pressures) (Carr et al. 2010).

Since polyphenols have a tendency to thermally degrade at high temperatures, the measurement of their aqueous solubilities above the boiling point of water is difficult (Srinivas and King 2010). Besides, solubility experiments can be unmanageable (i.e., time consuming and expensive) because it is extremely difficult to isolate the polyphenols at the levels of required purity. Usually, the polyphenol must first be extracted from plant tissues, then purified and isolated from other undesired compounds and finally, characterized in terms of its major molecular features. Although this entire procedure is widely covered in the literature (Mueller-Harvey 2001; Santos-Buelga and Williamson 2003; Naczk and Shahidi 2004; Serrano et al. 2009; Ignat et al. 2011; Khoddami et al. 2013) until now no standard or completely satisfactory methods to obtain pure polyphenols are available and their effectiveness strongly depends on their molecular complexity. For instance, extraction, purification, and isolation of tannins are quite dependent on their degree of polymerization (highly polymerized tannins are difficult to analyze) (Serrano et al. 2009). Therefore, scarce data on the solubility of polyphenols in PHW can be found in the literature. For instance, Srinivas et al.

(2010a, 2010b) measured the solubility of two phenolic acids (gallic acid hydrate and protocatechuic acid), a flavan-3-ol ((+)-catechin hydrate) and flavonols (quercetin and its dehydrate) in PHW using a dynamic flow apparatus coupled to a HPLC system designed to avoid thermal degradation of polyphenols. Results showed that the solubility of these polyphenols in PHW increase exponentially with temperature. Also, some data on the aqueous solubility of polyphenols (particularly those with simpler molecular structures) at atmospheric conditions can be found in the literature. Noubigh et al. (2007b) and Queimada et al. (2009) have determined the aqueous solubility of two particular polyphenols (vanillin and tyrosol, respectively) at temperature ranges below the normal boiling point and atmospheric pressure using standard shake-flask methods coupled to UV spectrophotometry or HPLC methods. Furthermore, several authors have measured the aqueous solubility of different phenolic acids such as gallic (Lu and Lu 2007; Daneshfar et al. 2008; Mota et al. 2008; Noubigh et al. 2008), vanillic, ferulic (Noubigh et al. 2007a), trans-cinnamic, caffeic (Mota et al. 2008), protocatechuic, syringic, o-coumaric, ellagic (Queimada et al. 2009), and salicylic acids (Nordström and Rasmuson 2006; Shalmashi and Eliassi 2007; Matsuda et al. 2008), using similar conditions and methods. In all these cases, solubility of polyphenols in water at atmospheric conditions also increases with temperature. Other methods can be found in literature to determine the experimental solubility of polyphenols at fixed conditions. For instance, Haslam (1996) compared the aqueous solubility of two similar tannins, castalagin and vescalagin, with that of the tannin β-1,2,3,4,6-penta-*O*-galloyl-D-glucose in terms of their octanol/water partition coefficient (K [octanol/water]) at 25°C and 1 atm. He found that castalagin and vescalagin were more water soluble, since they had a K [octanol/water] = 0.1, lower than the value for β-1, 2, 3, 4, 6-penta-*O*-galloyl-D-glucose (K [octanol/water] = 32). Tanaka et al. (2000) estimated the aqueous solubility of a polymeric tannin fraction extracted from Paeoniae Radix, an important crude drug in Chinese traditional medicine. They found that the polymeric fraction was 25% less soluble in water than in a 50% methanol solution by comparing the peak areas obtained after a HPLC analysis at 28°C.

The aforementioned difficulty to measure the solubility of polyphenols in PHW (and water in general) highlights the importance to generate correlation and prediction models. Two different approaches have been applied to accomplish such a goal: empirical equations and thermodynamic models. Empirical equations are useful to correlate the solubility of a solid solute by fitting nonphysical parameters to experimental data at given conditions of temperature and pressure. Most of the empirical equations used to correlate the solubility of polyphenols in water at pressurized or atmospheric conditions are based on modifications of the Williamson (1944) and Miller et al. (1998) equations and correlations from Van't Hoff plots. For instance, Srinivas and coworkers (Srinivas et al. 2010a, 2010b) applied simplified versions of the Williamson (also known as Apelblat equation) and Miller equations to describe the solubility data of some

phenolic acids and flavonoid compounds in PHW. Lu and Lu (2007) have adapted the Richards equation (Richards 1959) to describe the S-type curve of the solubility of gallic acid in water at atmospheric conditions as a function of temperature. Other authors (Nordström and Rasmuson 2006; Noubigh et al. 2007a) have derived particular empirical correlations from Van't Hoff plots to correlate the aqueous solubility of different phenolic acids.

Results obtained with empirical equations are only valid within the temperature and pressure conditions they were evaluated. Besides, empirical equations require a lot of experimental solubility data to fit their parameters. Therefore, they are not useful for extrapolation and prediction of new data. An adequate alternative is to use a thermodynamic model for calculating the solubility of a solid solute in a given solvent by (Prausnitz et al. 1998),

$$\ln x_1^L = \frac{\Delta_{fus}h}{RT_{tr}}\left(\frac{T_{tr}}{T}-1\right)-\frac{\Delta c_p}{R}\left(\frac{T_{tr}}{T}-1\right)+\left(\frac{\Delta c_p}{R}\right)\ln\frac{T_{tr}}{T}-\gamma_1(T,P,x_1^L) \tag{3.1}$$

which is obtained following a straightforward derivation from the isofugacity (equacondition of solid–liquid phase equilibrium [SLE]) and considering the case of SLE where the liquid phase is a mixture of dissolved solute and solvent, and the solid phase does not contain any solvent. In equation 3.1, x_1^L is the solute solubility, T and P are the temperature and pressure, R is the ideal gas constant, γ_1 is the activity coefficient of the compound in the liquid phase, T_{tr} is the triple point temperature and $\Delta c_p = cp_{(liquid)} - c_{p(solid)}$ is the change in the heat capacity of the solute. Since the triple point temperature and the normal temperature of fusion are similar, T_{tr} can be replaced by the temperature of fusion, T_{fus}; $\Delta_{fus}h$ refers to the enthalpy of fusion at that temperature. Moreover, Δc_p at T_{fus} can be considered equal to zero, which is an assumption commonly used for the estimation of solubility (Prausnitz et al. 1998). This assumption is based on empirical observations, and its success depends on the chemical structure of the compound, its physical properties, and the temperature of the system. By considering these simplifications, equation 3.1 becomes,

$$\ln x_1^L = -\frac{\Delta_{fus}h}{R}\left(\frac{1}{T}-\frac{1}{T_{fus}}\right)-\ln\gamma_1(T,P,x_1^L) \tag{3.2}$$

which provides a route to calculate the solubility of a given compound by solving numerically for x_1^L at given conditions of temperature and pressure. The molar enthalpy of fusion of the pure solute, and the temperature of fusion of the solute, are usually obtained from literature or determined through group contribution methods (Marrero and Gani 2001), while the activity coefficient of the solute in solution, γ_1, is usually determined with thermodynamic models. Most of the thermodynamic models dealing with the aqueous solubility of polyphenols are

based on activity coefficient approaches such as UNIFAC (Fredenslund et al. 1975), A-UNIFAC (Ferreira et al. 2003, 2005), modified UNIQUAC (Larsen et al. 1987; Peres and Macedo 1996), NRTL (Renon and Prausnitz 1968), and NRTL-SAC (Chen and Song 2004; Chen and Crafts 2006). These approaches have been successfully used to calculate the aqueous solubility of several polyphenols (mostly phenolic acids) at atmospheric pressure and temperatures below the normal boiling point of water (Queimada et al. 2009; Mota et al. 2012). Although activity coefficient models are adequate to describe the aqueous solubility of polyphenols at atmospheric conditions, no applications of this approach were found in the literature to model the solubility of polyphenols in PHW.

More promising thermodynamic models to tackle this challenge are those that explicitly take into account the effects of molecular structure and intramolecular interactions of polyphenols and their specific association with water (e.g., hydrogen bonding) on their aqueous solubility. The CPA (Kontogeorgis et al. 1996) and SAFT-type (Chapman et al. 1990; Huang and Radosz 1990, 1991; Gil-Villegas et al. 1997; Galindo et al. 1998; Gross and Sadowski 2001, 2002) equations of state (EoS) satisfy such requirements. Both EoS have been successfully applied for modeling the solubility (SLE) of a wide range of nonassociating, associating, polar, and polymer systems (Pan and Radosz 1999; Kontogeorgis et al. 2006; Tumakaka et al. 2007; Cameretti and Sadowski 2008; Kiesow et al. 2008; Grosse Daldrup et al. 2009; Ruether and Sadowski 2009; Cuevas et al. 2011), but only CPA has been used to calculate the aqueous solubility of polyphenols. For instance, Mota, Queimada, and coworkers (Mota et al. 2008, 2010; Queimada et al. 2009) adequately correlated the solubility of phenolic acids and vanillin in water at atmospheric pressure and temperatures below 100°C using the CPA EoS. No CPA or SAFT applications were found in literature for estimating the solubility of polyphenols in PHW, which represents an opportunity for future research.

3.4.2 Key parameters for optimizing the PHWE of polyphenols

In the PHWE of polyphenols, the temperature and extraction time define the total extraction yield, polyphenol content, and composition and bioactive properties (fundamentally the antioxidant activity) of the extracts, which are strictly related to the efficiency of the process. PHWE of phenolic compounds is a complex process where several phenomena appear such as thermal degradation, selective extraction of polyphenols, and the formation of neo-antioxidant and toxic compounds (Martins et al. 2000; Yilmaz and Toledo 2005), which are highly dependent on temperature and extraction time (Rodriguez-Meizoso et al. 2006; Duan et al. 2009; Plaza et al. 2010b, 2010c; Srinivas et al. 2011).

Since polyphenols are compounds sensitive to high temperatures, especially above 100°C (Nakamura et al. 1998; Palma et al. 2001; Srinivas et al. 2011), the extraction yield of these specific compounds during PHWE will be determined by both their solubility and their degradation rate at the fixed operating

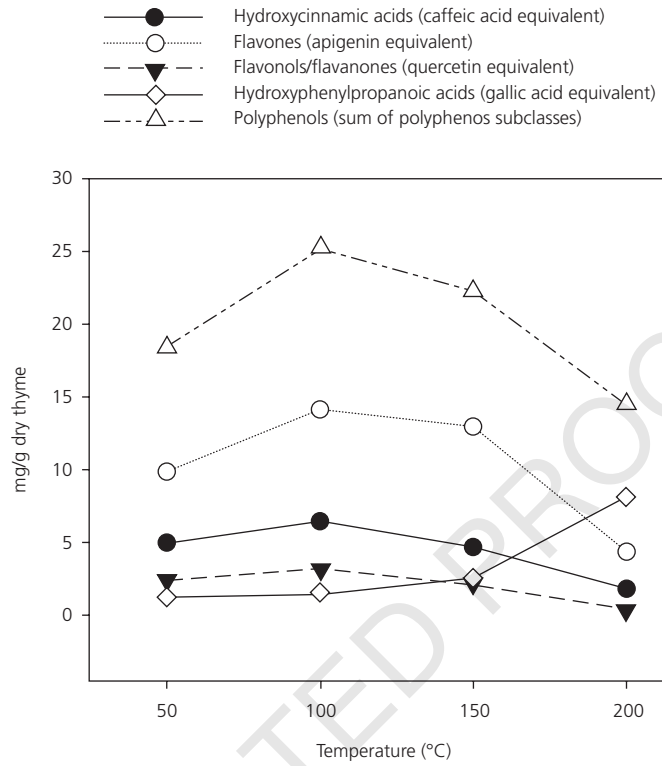

Figure 3.4 Extraction of polyphenol subclasses from deodorized thyme obtained at different temperatures and at 15 minutes. Data adapted from Vergara-Salinas et al. (2012).

temperature and time. Explaining it simply, the polyphenols' solubility in water and then their extraction yield increase as the temperature and time increase up to a certain range at which thermal degradation becomes predominant. For instance, Vergara-Salinas et al. (2012) found that the extraction yields of total polyphenols, hydroxycinnamic acids, flavones, and flavonols/flavanones increased with temperatures up to 100°C in most of the extraction times tested. When increasing the temperature above 150°C, the recovery of these phenolic compounds decreased due to thermal degradation. Only the recovery of dihydroxyphenyllactic acid (a hydroxyphenylpropanoic acid) increased at temperatures above 100°C, probably as a product of the thermal degradation of rosmarinic acid. At 50°C the extraction yields of flavones and total polyphenols increased with extraction time, whereas those of flavonols and hydroxycinnamic acids remained practically the same. In turn, at 150°C, all polyphenolic yields were negatively affected by the exposure time. The evolution of the extraction yields at 15 minutes and different temperatures (50, 100, 150, and 200°C) are shown in Figure 3.4. Kumar et al. (2011) reported that the highest extraction yield of quercetin-3-galactoside, kaempferol, and isorhamnetin from seabuckthorn

leaves was at 150°C (temperature range of study from 50 to 200°C). Rangsriwong et al. (2009) studied the PHWE of gallic acid, ellagic acid, and corilagin from *Terminalia chebula* Retz fruits between 120 and 220°C. The extraction of gallic acid and ellagic acid increased with the extraction temperature up to a maximum at 180°C, whereas the highest amount of corilagin was recovered at 120°C. In the PHWE of phenolics from red grape skin, Ju and Howard (2005) reported that increasing the temperature from 100 to 110°C produced an increase in the extraction of anthocyanins, although extraction temperatures above 110°C resulted in lower contents of individual and total anthocyanins. In the PHWE of tannins from grape seeds, increasing the extraction temperature caused an increase in the tannin extraction yield, peaking at 150°C (García-Marino et al. 2006). Although tannins are more thermo-stable than most of the other polyphenols, probably due to their polymeric structure (Larrauri et al. 1997), extraction temperatures above 150°C may cause their degradation (Gaugler and Grigsby 2009).

Due to the different polarities, polyphenols could be extracted selectively by PHWE. Rodriguez-Meizoso and coworkers (2006) studied the selective PHWE of polyphenols from oregano leaves (*Origanum vulgare* L.) at several temperatures. The extracts obtained at different temperatures were analyzed by HPLC-DAD. Most identified compounds were from the flavanone and dihydroflavonol subclasses. Flavonols were also found in the form of quercetin and, in lesser amounts, flavones. At the lowest temperature, the more polar compounds, flavanones and dihydroflavonols were preferentially extracted. The extraction of the less polar compounds was highly favored when temperature increased up to 200°C. Ibañez et al. (2002) also studied the selective recovery of antioxidant compounds from rosemary by PHWE. Results indicate high selectivity of PHW for the most active compounds of rosemary: carnosol, rosmanol, carnosic acid, methyl carnosate, cirsimaritin, and genkwanin. Depending on the extraction temperature, the extracts showed different compound profiles (Figure 3.5). Carnosol, rosmanol, and genkwanin were preferentially extracted at 100°C. At 200°C, the extraction of carnosic acid, methyl carnosate, and cirsimaritin was favored.

Other types of antioxidant compounds can also be found in the extracts obtained at high temperatures, particularly products from Maillard, thermoxidation, and caramelization reactions. For instance, Plaza et al. (2010a) found that the formation of Maillard products (fluorescent advanced glycated end products) and browning products (e.g., melanoidins) are significantly favored at 200°C compared to 100°C. Kulkarni et al. (2008), who studied the PHWE of antioxidants from *Eucaliptus grandis*, found that the main antioxidant compounds obtained in the extracts were pyrogallol, 5-hydroxymethyl-2-furaldehyde (HMF), and 4,4,6,6-tetramethyl-3,5-dioxo-cyclohex-1-enecarboxylic acid, which were not originally present in the untreated plant. Apparently these compounds were formed through degradation reactions generated by the high reactivity of

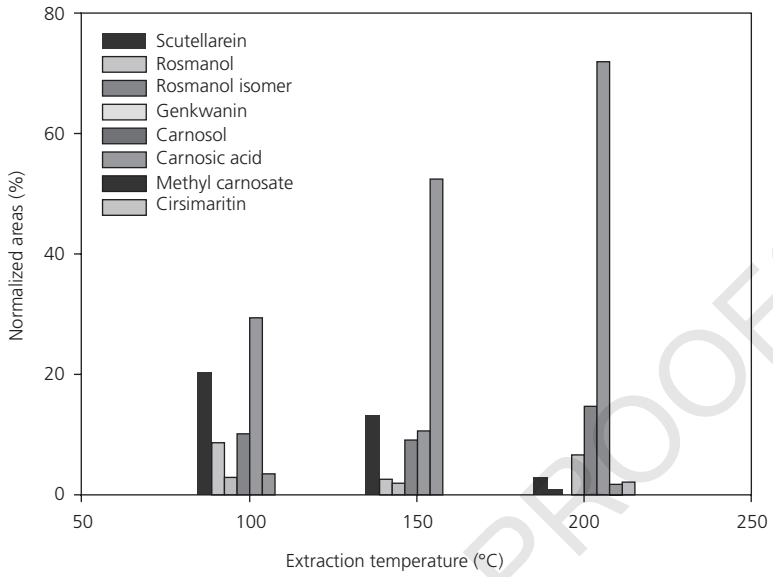

Figure 3.5 Selective recovery of antioxidant compounds from rosemary by PHWE. Data adapted from Ibañez et al. (2002). Normalized areas were obtained by GC-MS analysis.

water at high temperatures. In the PHWE of pomegranate, He et al. (2012) also studied the formation of Maillard reaction, particularly the content of HMF in the extracts. The results indicated that intermediate Maillard reaction products increased with temperature up to a maximum at 220°C and decreased when temperature was higher than 240°C, whereas the formation of final Maillard reaction products increased constantly with the extraction temperature. In particular, the HMF content in the extracts increased more than 10 times when the extraction temperature was raised from 100 to 220°C. At temperatures higher than 220°C, the HMF content decreased due to its degradation.

Temperature and extraction time also affect the bioactivity of the polyphenolic extracts obtained from plant matrices by PHWE. Specifically, both parameters have a strong effect on the antioxidant activity of the extracts. In general, antioxidant activity increases with the extraction temperature (Rodriguez-Meizoso et al. 2006; Baek et al. 2008; Herrero et al. 2010; Kumar et al. 2011; Vergara-Salinas et al. 2012), mainly because the solubility and diffusion rate of several polyphenols is enhanced. However, at high temperatures the formation of antioxidant compounds from Maillard, thermoxidation, and caramelization reactions occurs. For instance, He et al. (2012) observed that the HMF behavior coincides with trend of antioxidant activity (Figure 3.6), showing the significant contribution of the new antioxidant formed at high temperatures to the antioxidant activity of the extract. Additionally, products from the thermal decomposition of polyphenols (e.g., caffeic acid) and lignocellulose during the PHWE of various plant matrices have revealed high antioxidant activity (Guillot

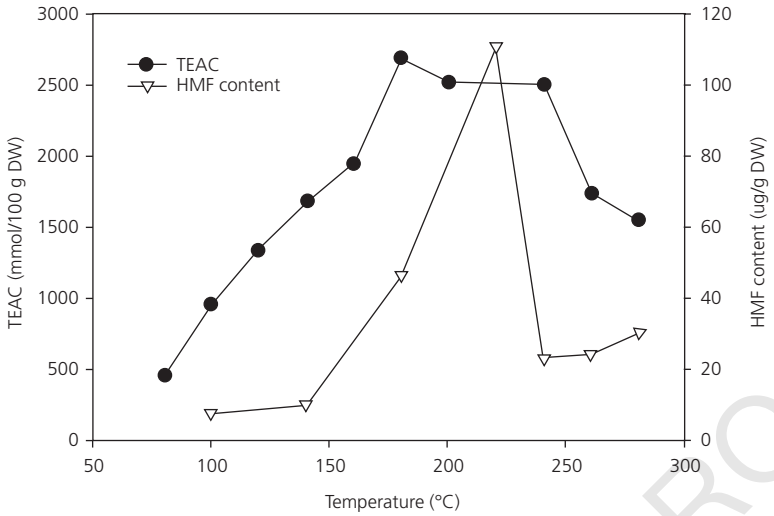

Figure 3.6 Relationship between the increase in the antioxidant activity (Trolox equivalent antioxidant capacity [TEAC]) and the formation of hydroxymethylfurfural (HMF; a Maillard reaction product) in the pressurized hot water extraction of polyphenols from pomegranate. Data adapted from He et al. (2012). DW, dry extract.

et al. 1996; Chen and Ho 1997; Wahyudiono et al. 2008; Hendriks and Zeeman, 2009). Although Maillard reaction products strengthen the antioxidant activity of the extracts obtained by PHWE, they can also be toxic, mutagenic, and carcinogenic (Martins et al. 2000; Yilmaz and Toledo 2005; Husøy et al. 2008). Therefore, care should be taken when maximizing the antioxidant activity of plant extracts obtained through PHWE. Plaza et al. (2013) made an interesting study evaluating the effect of the temperature and time on the flavonols recovery, antioxidant activity, and formation of Maillard reaction products in the PHWE of apple by-products. By using the response surface methodology, they determined the optimum condition for flavonols extraction (120°C and 3 minutes) as well as the condition that maximizes the antioxidant activity and minimizes the formation of Maillard reaction products (125°C and 3 minutes).

Additionally, since increasing the extraction temperature also causes an increase in the capacity of water to solubilize and hydrolyze several components of plant materials, a great amount of diverse compounds can be released during PHWE (Herrero et al. 2006b, 2010; Ong et al. 2006; Plaza et al. 2010a). At temperatures of 160°C and higher, pressurized hot water is able to solubilize hemicellulose (Ingram et al. 2009) and lignin (Liu and Wyman 2003). Moreover, during a water-based thermal process, part of the hemicellulose is hydrolyzed and forms acids. These acids are assumed to catalyze hydrolysis of remaining hemicelluloses (Gregg and Saddler 1996). For instance, Vergara-Salinas et al. (2012) found that the total extract obtained from grounded deodorized thyme leaves by PHWE increased with temperatures up to 200°C

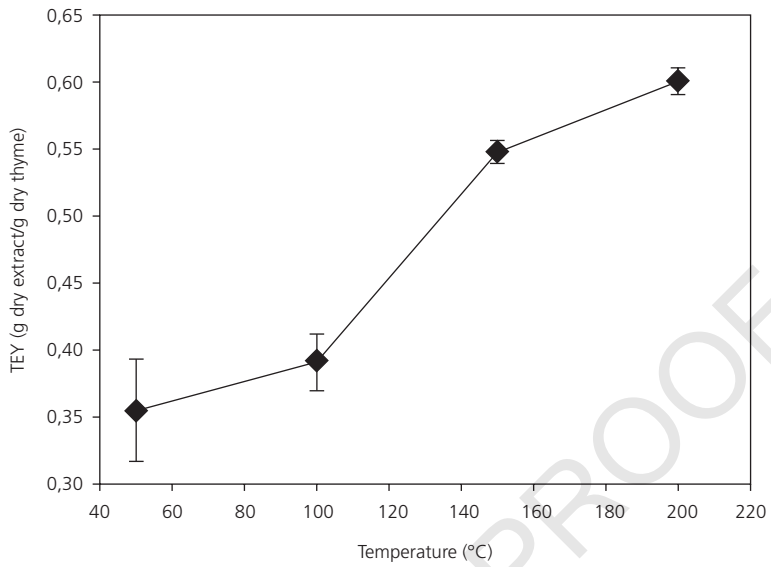

Figure 3.7 Increase of the total extraction yield (TEY) with temperature in the PHWE of polyphenols from deodorized thyme. Data adapted from Vergara-Salinas et al. (2012).

(Figure 3.7.) Additionally, hydrolysis of lignocellulosic material in PHWE of polyphenol-rich materials, which is usually overlooked, may contribute to the release of phenolic cell wall–associated compounds (Pérez-Jiménez and Torres 2011). Also, the lignocellulose hydrolysis contributes to obtain sugars, a raw material for several processes (e.g., conversion to biofuels) (Yu et al. 2007).

3.4.3 Equipment and modes of operation in the PHWE of polyphenols

The system described before in Figure 3.3 has been widely applied for the PHWE of polyphenols from plant material using laboratory-scale equipment. For instance, homemade units have been used for the PHWE of flavonoids from aspen knotwood (Hartonen et al. 2007) and phenolic compounds from potato peels (Singh and Saldaña 2011). However, most of the applications are based on commercially available accelerated solvent extractors (ASEs) developed by Thermo Scientific Dionex (Salt Lake City, UT), which have been used for obtaining phenolic extracts from agro-industrial by-products (Co et al. 2009; Herrero et al. 2011; Ko et al. 2011; Vergara-Salinas et al. 2013) and herbs (Dawidowicz et al. 2009; Kumar et al. 2011; Vergara-Salinas et al. 2012). Although PHWE is a straightforward scalable process from data gathered in small-scale experiments (Pronyk and Mazza 2009), no applications were found in the literature for the pilot-scale and industrial-scale PHWE of polyphenols. However, apparatus designed for other industrial applications, such as those used for the remediation of contaminated soils (Lagadec et al. 2000), could be adapted and used for that

purpose. Also, specialized companies such as Thyssenkrupp-Uhde (Dortmund, Germany), Chematur Technologies (Karlskoga, Sweden), Flavourtech Pty. Ltd. (Griffith, Australia), and Critical Processes Ltd. (North Yorkshire, UK) could modify their high-pressure technologies or develop new ones for the industrial-scale PHWE of polyphenols. Particularly, an extraction pilot plant located at Critical Processes Ltd. and described in Clifford (2005) is ideal to develop industrial PHWE processes.

PHWE of polyphenols is mainly carried out in a static manner. If phase equilibria is reached in this mode (i.e., the polyphenol of interest is completely solubilized in water), the efficiency of the process will not increase beyond this point and the optimization of the extraction time becomes fundamental (Herrero et al. 2013). However, several batch extraction cycles with replacement of pressurized hot water can be used to surpass this limit. Most of the literature cited in this chapter (which fundamentally uses laboratory-scale equipment) deals with this static extraction mode. For instance, Plaza et al. (2013) have extensively studied the static PHWE of several antioxidant polyphenols from apple by-products.

Dynamic extraction mode has also been used for the PHWE of polyphenols, but to a lesser degree. For instance, Ho et al. (2008) analyzed the dynamic PHWE of lignans from flaxseed meal. They reported that internal mass transfer was the controlling factor in the process since changing the flow rate had no effect on the extraction rate. Rangsriwong et al. (2009), who studied the dynamic PHWE of polyphenols from *Terminalia chebula* Retz. fruits, demonstrated that the extraction rate of the target compounds was influenced by external mass transfer given that the extraction increased with an increase in the volumetric flow rate from 2 to 3 or 4 mL/min. One of the main advantages of using dynamic PHWE instead of the static mode would be related to the thermal stability of polyphenols: the continuous flow of water through the extraction cell of a dynamic system contributes to avoid the thermal degradation of polyphenols (Ibañez et al. 2012).

Commercial laboratory-scale equipment commonly used for the PHWE of polyphenols (Dionex ASE) can only be operated in static (batch) mode. In turn, homemade equipment can be used in a flexible manner to perform both dynamic and static extractions (Ibañez et al. 2012). A good example of homemade dynamic equipment is the semicontinuous system developed by Monrad et al. (2012) to extract several polyphenols from grape pomace. Unlike the typical system shown in Figure 3.3, the extraction cell is placed outside the oven to avoid excessive exposure of the sample to high temperature and hence prevent its decomposition. Continuous PHWE processes are poorly covered in the literature. For instance, Soto Ayala and Luque de Castro (2001) successfully developed a continuous PHWE system to isolate essential oils rich in phenolic terpenes from ground oregano leaves. Technologies from the aforementioned companies (Thyssenkrupp-Uhde, Chematur Technologies, Flavourtech Pty. Ltd., and Critical Processes Ltd.) can be adapted to develop a continuous PHWE process. For instance, the Integrated Extraction System (IES) from Flavourtech Pty. Ltd.,

which has been used to obtain flavors and extracts from tea leaves and coffee beans at normal conditions, is an interesting alternative. IES is equipment consisting of five modules (slurry preparation, flavor extraction, clarification, washing, and concentration) that pretreats the raw plant material by milling and mixing it with water to generate a slurry, performs the extraction of volatile flavor compounds from the slurry using a countercurrent water flow, and clarifies and concentrates the flavor-stripped slurry to obtain the desired extract.

3.4.4 PHWE of different polyphenols from plant sources

In the last few years there has been an increase in the studies on PHWE of phytochemicals from plants and fruits, especially polyphenols. In particular, aromatic herbs and agro-industrial by-products have been extensively explored as sources of polyphenols (Table 3.2). PHWE of essential oils rich in phenolic terpenes, flavonoids, phenolic acids, and condensed tannins are discussed in the next subsections.

PHWE of essential oils

Several studies confirmed that many leafy spices and medicinal herbs, especially those belonging to the *Lamiaceae* family such as sage, rosemary, oregano, and thyme, show strong antioxidant activity (Kahkonen et al. 1999; Ong et al. 2006). The main bioactive compounds of medicinal herbs may be divided in: (1) essential oils, which contain a mixture of oxygenated compounds such as phenolic terpenes and hydrocarbons, and (2) nonvolatile phenolic compounds such as flavonoids and phenolic acids (Zheng and Wang 2001; Ibañez et al. 2002). In general, PHWE present several advantages over traditional extraction techniques for obtaining essential oils: low extraction times, high quality, low costs and environmentally friendly (Basile et al. 1998; Fernandez-Perez et al. 2000; Gámiz-Gracia and Luque de Castro 2000; Kubátová et al. 2001; Soto Ayala and Luque de Castro 2001; Herrero et al. 2006a). Basile et al. (1998) studied the principles involved in the PHWE process of essential oil from *Rosmarinus officinalis* (rosemary). The most water-soluble compounds were removed rapidly and high temperatures increased the extraction rate. The extraction performance and cost were compared with those obtained from a typical process of steam distillation. A higher amount of oxygenated compounds was obtained by PHWE (with similar energy and water costs). However, the extraction of monoterpenes, hydrocarbons, and large lipids was less efficient. Similar results were found by Kubátová et al. (2001) in the PHWE of essential oils from savory and peppermint.

PHWE of flavonoids and phenolic acids

PHWE present several features that make it an attractive alternative to traditional organic solvent extraction for the recovery of polyphenols from plant materials: low cost, fast, temperature-dependent selectivity, human and environmentally

Table 3.2 Main references on PHWE of polyphenols published during the last 15 years. Details about sources of extraction, their principal compounds (fundamentally polyphenols), and methods of analysis used to identify them are included.

Source	Principal compounds	Method of analysis	Reference
Herbs, spices, and shrubs			
Clove buds (*Syzygium aromaticum*)	Eugenol and eugenyl acetate	GC-MS	(Rovio et al., 1999)
Deodorized thyme leaves (*Thymus vulgaris*)	Hydroxycinnamic acids, flavones, flavonols, and flavanones	Folin-Ciocalteu assay FRAP assay ORAC assay DPPH radical assay HPLC-MS/MS	(Vergara-Salinas et al., 2012)
Hops samples (*H. lupulus* L.)	Prenylflavonoids	Folin-Ciocalteu assay Anti-inflammatory activity HPLC-DAD HPLC-MS/MS	(Gil-Ramírez et al., 2012)
Gastrodia elata Blume	Gastrodin and vanillyl alcohol	HPLC–DAD HPLC–MS/MS RP-HPLC-UV	(Teo et al., 2008)
Licorice roots (*Glycyrrhiza uralensis* Fisch)	Glycyrrhizin, glycyrrhetic acid, and liquiritin	DPPH radical assay Reducing Power by Oyaizu method (Oyaizu, 1986) Folin-Ciocalteu assay HPLC-UV-vis	(Baek et al., 2008)
Milk thistle (*Silybum marianum*)	Taxifolin, silichristin, silidianin, silibinin, and isosilibinin	HPLC–DAD	(Duan et al., 2009)
Oregano leaves (*Origanum onites*)	Borneol, terpinen-4-ol, and carvacrol	GC-GC/ TOF/MS	(Ozel and Kaymaz, 2004)
Oregano leaves (*Origanum vulgare*)	Phenolic antioxidants flavanones, dihydroflavonols, favonols, and flavones	HPLC–DAD DPPH radical assay Folin-Ciocalteu assay	(Rodriguez-Meizoso et al., 2006)
Peppermint (*Mentha piperita*)	Oxygenated and nonoxygenated flavor and fragrance compounds	GC- FID	(Kubátová et al., 2001)

Rosemary leaves (*Rosmarinus officinalis*)	Oxygenated fragrance and flavor compounds	GC- FID	(Basile et al., 1998)
	Carnosol, rosmanol, carnosic acid, methyl carnosate, cirsimaritin, and genkwanin	GC-MS	(Ibañez et al., 2002)
	Rosmarinic acid, carnosic acid, caffeic acid, and carnosol (among others)	Folin-Ciocalteu assay DPPH radical assay UPLC-DAD-MS/MS	(Herrero et al., 2010)
	Total phenolic compounds Carbohydrates Proteins Maillard reaction products (melanoidins and advanced glycation end products) Antioxidants	Folin-Ciocalteu assay ABTS radical assay ORAC assay Superoxide radical scavenging capacity Fluorescence analysis Browning intensity DPPH radical assay Life cycle assessment	(Plaza et al., 2010) (Rodríguez-Meizoso et al., 2012)
Sage (*Salvia officinalis*)	Rosmarinic and carnosic acids, carnosol and methyl carnosate	HPLC/UV/ESI/MS DPPH radical assay	(Ollanketo et al., 2002)
Savory (*Satureja hortensis*)	Oxygenated and nonoxygenated flavor and fragrance compounds	GC- FID	(Kubátová et al., 2001)
Seabuckthorn leaves (*Hippophae rhamnoides*)	Quercetin-3-galactoside, kaempferol, and isorhamnetin	Folin-Ciocalteu assay FRAP assay Total reducing power Cytotoxicity and antioxidant activity in cell culture model HPLC-UV	(Kumar et al., 2011)
Tea leaves (*Camellia sinensis*)	Catechin and epicatechin	HPLC-UV-vis	(Piñeiro et al., 2004)
Thyme leaves (*Thymus vulgaris*)	Total phenolic compounds Carbohydrates Proteins Maillard reaction products (melanoidins and advanced glycation end products)	Folin-Ciocalteu assay ABTS radical assay ORAC assay Superoxide radical scavenging capacity Fluorescence analysis Browning intensity	(Plaza et al., 2010)

(*Continued*)

Table 3.2 (*Continued*)

Source	Principal compounds	Method of analysis	Reference
Verbena (*Verbena officinalis*)	Total phenolic compounds Carbohydrates Proteins Maillard reaction products (melanoidins and advanced glycation end products)	Folin-Ciocalteu assay ABTS radical assay ORAC assay Superoxide radical scavenging capacity Fluorescence analysis Browning intensity	(Plaza et al., 2010)
Fruits, seeds, and vegetables			
Bitter melon fruits (*Momordica charantia*)	Catechin, gallic acid, gentisic acid, and chlorogenic acid	ABTS radical assay Folin-Ciocalteu assay HPLC-UV	(Budrat and Shotipruk, 2009)
Defatted flaxseed meal (*Linum usitatissimum*)	Lignans	HPLC–DAD	(Ho et al., 2007)
Defatted rice bran (*Oryza sativa*)	Total phenolics compounds Carbohydrates Proteins Furfural	Folin-Ciocalteu assay DPPH radical assay Antioxidative activity for autoxidation of linoleic acid	(Wiboonsirikul et al., 2007)
	Gallic acid, caffeic acid, *p*-coumaric acid, and ferulic acid	Folin-Ciocalteu assay HPLC UV–vis	(Fabian et al., 2010)
Defatted soybean flakes	Isoflavones	HPLC-UV-vis	(Li-Hsun et al., 2004)
Flaxseeds (*Linum usitatissimum*)	Lignans and other phenolics	HPLC-DAD	(Cacace and Mazza, 2006a, 2006b)
Onion	Quercetin-3,4-O-diglucoside, (2) quercetin-3-glucoside and quercetin-4-O-glucoside	DPPH radical assay HPLC–UV	(Andersson et al., 2012)
Soybean seeds	Isoflavones	HPLC–DAD	(Luthria et al., 2007)
Terminalia chebula Retz. fruits	Gallic acid, ellagic acid, and corilagin	Folin-Ciocalteu assay ABTS radical assay HPLC–DAD	(Rangsriwong et al., 2009)

Agroindustrial by-products			
Apple by-products	Polyphenols: 5-caffeoylquinic acid, hyperoside, isoquercitrin, reinutrin, phloridzin, avicularin, quercitrin, and quercetin. Maillard reaction products (melanoidins, furfural, and hydroxymethylfurfural)	Folin-Ciocalteu assay ABTS radical assay DPPH radical assay Analysis of Maillard reaction products HPLC-DAD	(Plaza et al., 2013)
Aspen knotwood (*Populus tremula*)	Naringenin, dihydrokaempferol, naringin, and taxifolin	GC–FID and GC–MS HPLC–UV and HPLC–MS	(Hartonen et al., 2007)
Citrus peels (*Citrus unshiu*)	Hesperidin and narirutin	HPLC and LC-MS/MS	(Cheigh et al., 2012)
Citrus pomace (*Citrus unshiu*)	Polymethoxylated flavones: sinensetin, nobiletin, and tangeretin	HPLC-UV-vis	(Kim et al., 2009)
Flooded gum leaves (*Eucalyptus grandis*)	Pyrogallol, 5-hydroxymethyl-2-furaldehyde, and 4,4,6,6-tetramethyl-3,5-dioxo-cyclohex-1-enecarboxylic acid	Radicals of peroxynitrite scavenging TLC analysis	(Kulkarni et al., 2008)
Grape pomace (*Vitis vinifera*)	Total phenolic compounds Total flavonoids	Folin-Ciocalteu assay DPPH radical assay Quantitative analysis of color intensity	(Aliakbarian et al., 2012)
	Anthocyanins and procyanidins	Polymeric Color HPLC-MS	(Monrad et al., 2012)
	Anthocyanins, proanthocyanidins, and polymeric pigments	Folin-Ciocalteu assay FRAP assay DPPH radical assay MALDI-TOF	(Vergara-Salinas et al., 2013)
Grape seeds (*Vitis vinifera*)	Catechin and epicatechin Catechins and proanthocyanidins	HPLC-UV-vis HPLC–DAD–MS	(Piñeiro et al., 2004) (García-Marino et al., 2006)
Grape skin (*Vitis vinifera*)	Anthocyanins	Folin-Ciocalteu assay Color density, polymeric color, and percent polymeric color ORAC assay HPLC-DAD	(Ju and Howard, 2003)

(*Continued*)

Table 3.2 (*Continued*)

Source	Principal compounds	Method of analysis	Reference
	Anthocyanins, flavonols, hydroxycinnamates, phenolic acids	ORAC HPLC-DAD HPLC-MS	(Ju and Howard, 2005)
	3-O-monoglucosides of delphinidin, cyanidin, petunidin, peonidin, and malvidin	Folin-Ciocalteu assay ABTS radical assay DPPH radical assay HPLC-DAD	(Šťavíková et al., 2011)
Mango leaves (*Mangifera indica*)	Mangiferin and quercetin 3-β-d-glucoside	DPPH radical assay HPLC–UV/vis	(Fernández-Ponce et al., 2012)
Olive leaves (*Olea europaea*)	Secoiridoids, tyrosols, hydroxycinnamic acid derivatives, and flavonoids	Folin-Ciocalteu assay ABTS radical assay DPPH radical assay LC-MS	(Herrero et al., 2011)
Onion skins	Quercetin, quercetin-4-O-glucoside kaempherol, isorahmnetin, and rutin	HPLC-UV	(Ko et al., 2011)
Orange peel	Anilines, phenols, and flavones	Subcritical water chromatography, UV detector	(Lamm and Yang, 2003)
Pomegranate peels (*Punica granatum*)	Punicalagin A and B (and their derivatives), ellagic acid (and their derivatives), and gallic acid Total phenolic and flavonoid content Condensed and hydrolyzable tannins	Folin-Ciocalteu assay DPPH radical assay Antioxidant activity using β-carotene-linoleate model system	(Çam and Hışıl, 2010)
Pomegranate seeds (*Punica granatum*)	Polyphenols: caffeic acid derivative, catechin and kaempferol 3-O-rutinoside (among others) Maillard reaction products (browning and hydroxymethylfurfural) and reducing sugar and free amino acid content	Folin-Ciocalteu assay ABTS radical assay DPPH radical assay Analysis of Maillard reaction products HPLC-ABTS (qualitative analysis of the individual antioxidants)	(He et al., 2012)

Potato peels	Gallic acid, chlorogenic acid, caffeic acid, protocatechuic acid, syringic acid, p-hydroxyl benzoic acid, ferulic acid, and coumaric acid	Folin-Ciocalteu assay HPLC-UV	(Singh and Saldaña, 2011)
White grapes (Viura variety)	Gallic acid, *p*-hidroxibenzoic acid, aesculetin, ferulic acid, scopoletin, sinapic acid and veratric aldehyde. caftaric acid, and *cis* and *trans*-coutaric acids	HPLC-DAD	(Palma et al., 2002)
Marine sources			
Microalgae (Chlorella vulgaris) and algae (Sargassum vulgare, Porphyra spp., Cystoseira abies-marina, Sargassum muticum, Undaria pinnatifida, and Halopitys incurvus)	Total phenolic compounds Carbohydrates Proteins Maillard reaction products (melanoidins and advanced glycation end products)	Folin-Ciocalteu assay ABTS radical assay ORAC assay Superoxide radical scavenging capacity Fluorescence analysis Browning intensity	(Plaza et al., 2010)
Microalgae (*Haematococcus pluvialis*)	Phenolic compounds	ABTS radical assay Antimicrobial activity HPLC-DAD HPLC–QqQ-MS GC-MS	(Rodriguez-Meizoso et al., 2010)

safe and efficient (Ju and Howard 2005; Budrat and Shotipruk 2009; Rangsriwong et al. 2009; Ko et al. 2011; Kumar et al. 2011; Cheigh et al. 2012). Budrat and Shotipruk (2009) compare PHWE with traditional solvent extraction methods (methanol extraction and Soxhlet water extraction) for the recovery of phenolic compounds from bitter melon. The antioxidant activity, the total phenolic content, and the amount of individual phenolic compounds (e.g., catechin, genistic acid, gallic acid and chlorogenic acid) increased when increasing extraction temperature. Particularly, the total phenolic compounds and individual phenolics in the extracts obtained by PHWE, especially at 200°C, were significantly higher than those in the extracts obtained by methanol extraction and Soxhlet water extraction. Moreover, the antioxidant activity of PHWE extracts was three times higher than the other extracts. Kumar et al. (2011) also reported pressurized hot water extracts of seabuckthorn with higher antioxidant activity and polyphenolic content (quercetin-3-galactoside, kaempferol, and isorhamnetin) than those obtained by Soxhlet and maceration methods. Similar results were found by Cheigh et al. (2012) for the extraction of flavanones from citrus peel (an agricultural by-product) when compared with conventional extraction methods using ethanol and methanol. In another work, Ju and Howard (2005) compared the PHWE of anthocyanins and other phenolics from grape skin (winery by-product) with conventional hot water or aqueous 60% (v/v) methanol extractions. The polyphenol content (anthocyanins, flavonols, hydroxycinnamates, and phenolic acids) and the antioxidant activity of the extracts obtained using pressurized hot water (between 110 and 160°C) were similar or slightly greater than those of the extracts obtained by conventional methods. However, the extraction time for the PHWE process was 10 times shorter.

PHWE of condensed tannins

Condensed tannins, also known as proanthocyanidins, comprise a group of polyhydroxyflavan-3-ol oligomers and polymers of flavanols that can be linked to other polyphenols such as phenolic acids and anthocyanins (Schofield et al. 2001; Negro et al. 2003; Haslam 2007). They can be found in high concentrations in grape seeds, plums, blackberries, cranberries, and choke berries among fruits; sorghums, pinto beans, and red kidney beans among cereals; hazelnuts and pecans among nuts; and ground cinnamon among spices. They are also present in beverages and snacks, such as red wine, grape juice, baking chocolate, and black chocolate, where they impart astringency and flavor (Gu et al. 2004; Xie and Dixon 2005).

García-Marino et al. (2006) studied the PHWE of proanthocyanidins from grape seeds and compared the results with a methanol/water extraction at atmospheric pressure. PHWE showed good extraction yield, in some cases better than the traditional hydroalcoholic extraction. They also found that even higher recoveries can be obtained with sequential extraction at 50, 100, and 150°C.

Monrad et al. (2010) found similar results when comparing PHWE at 140°C with conventional extraction (using acetone/water/acetic acid) in the recovery of proanthocyanidin monomers and oligomers from grape pomace. In liquid red grape extracts, proanthocyanidins can bind to anthocyanins to form polymeric pigments (Harbertson et al. 2003), another form of condensed tannins. Ju and Howard (2003) compared the PHWE (acidified) of phenolics from grape skin with the traditional Soxhlet extraction. They found that the extraction (or formation) yield of polymeric pigments with PHWE was higher than that of Soxhlet extraction with water and comparable to that obtained with a mixture of water-methanol. They also verified that the amount of polymeric pigments increases with temperature, especially above 100°C.

3.5 Conclusions

PHWE is a promising green extraction process for obtaining polyphenols from plant matrices. Using pressurized hot water as solvent presents several advantages over traditional extraction methods. Unlike commonly used solvents, water is nonflammable, nontoxic, readily available, and environmentally friendly. Its solvating properties can be profoundly improved by increasing temperature, which enhances the aqueous solubility of polyphenols and the diffusion process. This enhancement results in higher extraction yields and selectivities and shorter extraction times than conventional solvent extraction methods. In general, simple flavonoids (flavones, flavonols, flavanones, and anthocyanins) reach a maximum extraction yield at temperatures between 100°C and 120°C. Higher temperatures and long exposure times produce the degradation of these compounds. Polymeric flavonoids (condensed tannins) reach their maximum at about 150°C, evidencing a higher thermal stability, probably due to their polymeric structure. Some phenolic acids such as rosmarinic acid reach their highest extraction yield near 100°C and are degraded at higher temperatures. The extraction yield of other phenolic acids (e.g., gallic and dihydroxyphenyllactic acid) is maximized at temperatures above 150°C, partly due to their release from esterified polyphenols during their degradation.

High temperatures (above 100°C) and long exposure times would also favor the formation and release of polyphenol derivatives, nonpolyphenolic antioxidants, and toxic and mutagenic compounds with high antioxidant activity such as hydroxymethylfurfural. Hence, increasing extraction temperatures above 100 or 150°C causes a decrease in the extraction yield of polyphenols but a high recovery of total antioxidants. Consequently, the extracts obtained at high temperature processes such as PHWE cannot possibly be used without posttreatment. Further purification processes should be applied for obtaining safe products.

3.6 Future research

As we discussed in this chapter, aqueous solubility of polyphenols is a key parameter to design and optimize a PHWE process. Therefore, further studies on this topic should be carried out in the future. Particularly, experimental analysis of the solubility of fundamental polyphenols, such as flavanols and phenolic acids, are important to better understand the effect of temperature and pressure on their dissolution process. It is important to develop adequate thermodynamic models to describe and predict the solubility of specific polyphenols in water, which support the optimization of the PHWE process and reduce the amount of experimental data required.

Since nonpolyphenolic antioxidants and toxic and mutagenic compounds can be generated during the PHWE of polyphenols, it is required to deepen the main causes and dynamics of formation of these compounds and their effects on the quality of the extract and its bioactivity. Particularly, studies on the identification and isolation of the antioxidants (polyphenolic and nonpolyphenolic) present in the extracts become essential to control the PHWE process and improve the quality of the extract. This knowledge and the use of thermodynamic models for predicting solubility behaviors will contribute to develop pilot-scale or industrial-scale integral processes to extract polyphenols from plant materials, which would include PHWE and further purification and concentration units.

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