Intensification of bioactive compounds extraction from medicinal plants using ultrasonic irradiation

Renata Vardanega[1], Diego T. Santos[1,2], M. Angela A. Meireles[1]

[1]LASEFI/DEA/FEA (School of Food Engineering), UNICAMP (University of Campinas), SP, Brazil, [2]Industrial Process and Energy Systems Engineering (IPESE), Swiss Federal Institute of Technology Lausanne (EPFL), Lausanne, Switzerland

Submitted: 26-08-2013 Revised: 28-10-2013 Published: 10-06-2014

ABSTRACT

Extraction processes are largely used in many chemical, biotechnological and pharmaceutical industries for recovery of bioactive compounds from medicinal plants. To replace the conventional extraction techniques, new techniques as high-pressure extraction processes that use environment friendly solvents have been developed. However, these techniques, sometimes, are associated with low extraction rate. The ultrasound can be effectively used to improve the extraction rate by the increasing the mass transfer and possible rupture of cell wall due the formation of microcavities leading to higher product yields with reduced processing time and solvent consumption. This review presents a brief survey about the mechanism and aspects that affecting the ultrasound assisted extraction focusing on the use of ultrasound irradiation for high-pressure extraction processes intensification.

Key words: Bioactive compounds, extraction, high-pressure, process intensification, ultrasound

INTRODUCTION

Bioactive compounds are largely obtained from medicinal plants. Solid-liquid extraction is used in many chemical, biochemical and pharmaceutical industries for recovery bioactive compounds. Plants generally contain only a small amount of active compounds, but in most cases its high value justifies the development of the high-performance process. The need for effective extraction of bioactive compounds from plants without any loss of activity and high purity has resulted in development of newer process of extraction.[1,2]

Conventional extraction from plants comprises solid-liquid techniques depending usually upon organic solvents which present various shortcomings such as toxic residues, chemical transformation of extracts, use of a large quantity of organic solvents which are harmful to human and environment and long-term processing. In recent years, increases on the development of techniques that overcome these drawbacks with safer solvents have been observed. The use of ultrasound irradiation during the extraction procedure presents several advantages in terms of shortening the time of the process, decrease the volume of the extracting solvent and increasing the yield of the extraction in comparison with conventional methods.[1,3] In this paper, some principles and factors that influencing the ultrasound assisted extraction are presented. The next sections presents some recent applications of ultrasound coupled with extraction techniques under high-pressure, as well as results of mathematical modeling.

Address for correspondence:
Dr. Diego T. Santos, LASEFI/DEA/FEA (School of Food Engineering), UNICAMP (University of Campinas), Rua Monteiro Lobato, 80, 13083-862 Campinas, SP, Brazil.
E-mail: diego_tresinari@yahoo.com.br

Access this article online

Quick Response Code:

Website: www.phcogrev.com

DOI: 10.4103/0973-7847.134231

MECHANISM OF ULTRASOUND ASSISTED EXTRACTION

The intensification of extraction process using ultrasound has been attributed to the cavitation phenomena. The effects caused by the ultrasonic waves are compression and expansion cycles during the passage through the fluid. The expansion can create bubbles or cavities in a liquid. This is so when the negative pressure exerted exceeds the local tensile strength of the liquid, which varies depending on its nature and purity. The process by which vapor bubbles form, grow and undergo implosive collapse is known as cavitation.[4] The conditions within these imploding bubbles can be dramatic, with temperatures of 4500°C and pressures up to 100 MPa, which in turn produces very high shear energy waves and turbulence in the cavitation zone. The

combination of these factors (pressure, heat and turbulence) is used to accelerate mass transfer in the extraction process.[5]

Ultrasound also exerts a mechanical effect. In pure liquids, the bubble retains its spherical shape during the collapse, as its surroundings are uniform. However, when the bubble collapses near a solid surface it occurs asymmetrically and produces high-speed jets of solvent toward the cell walls. These jets have a strong impact on the solid surface, therefore, increasing the solvent penetration into the cell and increasing the contact surface area between solid and liquid phase [Figure 1].[4,6] Another effect caused by the ultrasound wave on the solid material is that the ultrasound waves can facilitate the swelling and hydration and so cause an enlargement in the pores of the cell wall. This will improve the diffusion process and therefore enhancing mass transfer.[7]

In general, the largest sonochemical effects are observed at lower temperatures, when majority of the bubble contents is in the gas. With a decrease in the vapor pressure of the mixture, there is an increase of the implosion intensity, thus increasing the ultrasonic energy produced upon cavitation.[8] The frequency of ultrasound also exerts significant influence on the yield and kinetic extraction. However, this influence depends of the medicinal plant structure and the target compound.[9]

The ultrasonic wave distribution inside an extractor is also a key parameter in the design of an ultrasonic extractor. The maximum ultrasound power is observed in the vicinity of the radiating surface of the ultrasonic horn. Ultrasonic intensity decreases rather abruptly as the distance from the radiating surfaces increases.[9] Furthermore, ultrasound intensity is attenuated with the increase of the presence of solid particles. In order to avoid standing waves or the formation of solid free regions for the preferential passage of the ultrasonic waves, additional agitation or shaking is usually used.[10]

FACTORS THAT AFFECTING ULTRASOUND ASSISTED EXTRACTION

Since the cavitation phenomenon is the principal responsible by the intensification of the extraction process, the parameters that affecting cavitation also affecting the extraction process performed under ultrasound effects. Besides the parameters intrinsically related to the ultrasonic devices (such as the frequency, wavelength and amplitude of the wave), the ultrasonic power (in kWh/L) and consequently intensity have also an effect on the extraction. The characteristics of the extraction medium as temperature and pressure, viscosity, surface tension, vapor pressure, besides nature and concentration of dissolved gas and presence of solid particles, if any, also determine the magnitude of the effect caused by the ultrasound in the extraction process and can affect not only the extraction yield but also the composition of the extract and consequently its biological properties.[3,5] We will discuss these factors in the following sections.

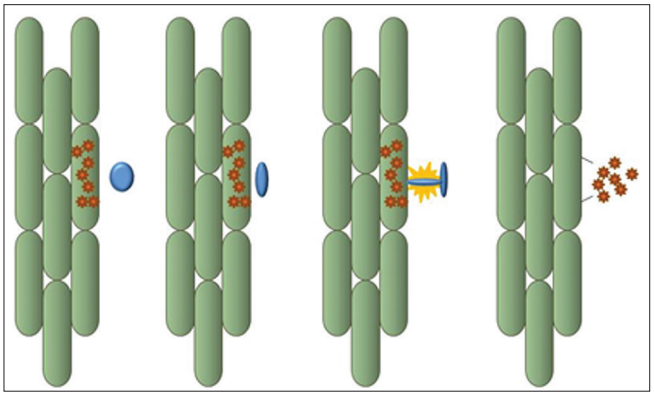

Figure 1: Collapse of cavitation bubble and release of plant content (adapted from Pingret *et al.*[3])

Ultrasonic power, intensity and density

The use of ultrasonics in industrial process has two main requirements; a liquid medium (even if the liquid element forms only 5% of the overall medium) and a source of high energy vibrations (ultrasound). The vibrational energy source is called transducer, which transfers the vibration (after amplification) to the so-called sonotrode or ultrasonic probe, which is in direct or indirect contact with the processing medium. However, the measurement of the actual acoustic energy applied in a sonochemical process is quite difficult. Sometimes, considering the different power level of the device, authors show the values of power applied as, for example, "20% of the total electric power capacity" and this is not as accurate measurement at all. In fact, in most of the ultrasound devices, the power measured is not proportional to the power step shown, leading to wrong conclusions or irreproducible results.[5,11]

Even knowing the ultrasonic power actually applied, it is difficult to compare the effects because often the results are not only reported on the different basis, but are also influenced by the geometry of the extractor. For instance, to report data indicating only the power applied is not enough. Indicating the power intensity (W/cm^2) or the power density (W/cm^3) is more appropriate.[11,12]

The intensity or amplitude of waves is used to classify the industrial applications: Low-intensity ultrasound with $<1\ W/cm^2$ and high-intensity ultrasound with 10-1000 W/cm^2.[13] The power density takes account the vessel volume which the ultrasound acts and it is very important, especially for the case of ultrasonic baths, where the whole bath volume should be considered. In addition, when the processing intended to be scalable, power density should be considered, that takes in to account extremely different acoustic streams and the corresponding difference results in the new volume.[5,11]

Medium pressure

The cavitation effects in ambient liquids are well-known and their application to conventional solvent extraction is well-established. However, when a liquid is pressurized, the acoustic intensity required to produce cavitation also increases and this generally

places a natural limitation on application of ultrasonics to high-pressure processes. In ordinary solvents, cavitation does not occur at elevated pressures.[14]

To initiate the growth of a cavitation bubble, an acoustic pressure above the so-called Blake threshold pressure (P_B) has to be applied.[15] Eq. 1 assumes that the static gas pressure (P_0), the vapor pressure (P_v), the surface tension (σ) and the equilibrium radius of the bubble (R_0) determine the required negative pressure in the liquid medium to start the explosive growth of a cavity.

$$P_B = P_0 - P_v + \frac{4}{3} \times \sigma \times \sqrt{\frac{2}{3} \times \frac{\sigma}{\left(P_0 + 2 \times \frac{\sigma}{R_0} - P_v \right) \times R_0^3}} \quad (1)$$

During pressurization of a liquid, the Blake threshold pressure increases, which imply that higher acoustic pressures are needed to produce cavitation. Obviously, no cavitation occurs when the Blake threshold pressure exceeds the maximum acoustic pressure.[16] Kuijpers *et al*.[17] showed sonoluminescence evidence for the occurrence of cavitation in CO_2 at 7.5 MPa and 10°C which is well below the critical temperature of CO_2. These authors argue that the high vapor pressure and low surface tension of the fluid counteracts the external pressure applied. They demonstrated that the threshold pressure of liquid CO_2 at 5.82 MPa is equal of the threshold pressure of water at 0.1 MPa and 20°C. The phenomenon was further studied by the same group and published by Kemmere *et al*.[16] who observed that the cavitation collapse of a bubble was not strong enough to create hot-spots for monomolecular conversion in bulk free-radical polymerization of methyl methacrylate using CO_2.

Although cavitation has thus been established in near-critical carbon dioxide, the absence of phase boundaries would appear to prohibit bubble formation above the critical point. This would imply that rate enhancement of supercritical fluid extraction (SFE) process can occur only through the turbulence associated with acoustic streaming or through simple mechanical vibration.[18]

In contrast, Thompson and Doraiswamy[19] pointed that an increase in the ambient reaction pressure generally results in an overall increase in the sonochemical effects due to the decrease in the vapor pressure of the mixture. Decreasing the vapor pressure increases the intensity of the implosion, thus increasing the ultrasonic energy produced upon cavitation. However, to observe this effect, the threshold pressure should be exceeded.

Extracting solvent physical properties

The selection of the best extracting solvent for ultrasound assisted extraction normally depends on its physical properties (surface tension, viscosity and vapor pressure) because these properties affect the cavitation intensity in a liquid phase.[1] Although the cavities are more easily formed with a solvent that has a high vapor pressure, low viscosity and low surface tension, the cavitation intensity increases for solvents with low vapor pressure, high viscosity and high surface tension.[19] The intermolecular forces in the liquid must be overcome in order to form the bubbles. Thus, solvents with high densities, surface tensions and viscosities generally have a higher threshold for cavitation but more harsh conditions once cavitation begins.[20]

Kuijpers *et al*.[17] calculated that the threshold pressure of the liquid CO_2 equals that of atmospheric water at 5.82 MPa and 20°C. For water at 5.82 MPa, a very high acoustic pressure is required to create cavitation. The threshold pressure in water is determined only by the static pressure and the surface tension of the liquid, because of its low vapor pressure. Because the vapor pressure does not change significantly with increasing temperature, the threshold pressure of water is approximately constant. On the other hand, since CO_2 condenses at a substantially higher pressure, its vapor pressure has a substantial influence.

Moreover, the cavitation phenomenon leads to the formation of highly reactive species that lead to chemical reactions. These effects starts during the collapse of the cavities in pure aqueous systems, gaseous water molecules entrapped in expanded microbubbles are fragmented as in pyrolysis and the mainly species formed are OH radicals. In aqueous media containing volatile organic gases and solutes, cavitation collapse not only results in the scission of water molecules to hydroxyl and hydrogen radicals, but also in the formation of organic radicals.[20-22]

Furthermore, cavitation can increase the reaction rates of existing process or start new reaction mechanisms by the formation of other reactive radical species. Those statements could suggest dramatic changes in the parameters as temperature or pressure of the bulk surrounding but this is not the case because the time scale for these microreactions is too small to affect cellular structure and enhance mass transport.[11,23] Balachandran *et al*.[18] studied the ultrasonic enhancement of the supercritical extraction from ginger and performed some tests for prove the effects of cavitation. As initiation of polymerization reactions by free radicals formed during cavitation is an established technique under ambient conditions, experiments were performed to determine if polymerization could be initiated by sonication in CO_2 at supercritical conditions. The results showed no polymerization of methyl methacrylate. The authors concluded either that there could be no cavitation collapse to generate free radicals or the collapse of the cavitation bubble is very weak and unable to create hot spots and induce radical formation.

Presence of dissolved gas in the medium

The type of radicals formed also depends on the presence and gas type dissolved in the medium. The gases act as nucleation sites for cavitation and then bubbling gases through the mixture facilitates the production of cavitation bubbles, but the type of gas used is important. In general, gases with high specific heat ratio give a greater cavitation effect than one with low specific heat ratio.

Monoatomic gases (i.e. argon and helium) convert more energy upon cavitation than diatomic gases (i.e. oxygen) due to the larger ratio of specific heats. Thompson and Doraiswamy[19] and Adewuyi[20] provided these and more information about the presence and nature of the dissolved gases on cavitation and reactions under ultrasound effects.

RECENT APPLICATIONS OF ULTRASOUND FOR HIGH-PRESSURE EXTRACTION PROCESSES

The combination of techniques, which can provide synergistic effects based on the similarity in the controlling mechanisms or supplementary roles, can be a viable option with possible commercial applications. This approach meets to the environmentally friendlier concept of saving resources by optimization of process conditions and/or introducing a new process technologies to preparations of valuable compounds.[1] Ultrasound-assisted process can be conveniently coupled with other techniques that are performed under high-pressure such as the extraction processes: Supercritical fluid extraction (SFE and pressurized liquid extraction (PLE).

Ultrasound assisted supercritical fluid extraction

The use of supercritical fluids as solvents is an interesting alternative for obtaining natural products with high quality without generating toxic residues. The usage of this technology increased rapidly, with new applications being developed almost every day.[24] Extraction with supercritical carbon dioxide is also considered as environmentally friendly technology which has gained acceptance as an alternative to conventional solvent extraction because its important advantages such as non-toxic, recyclable, cheap, relatively inert and non-flammable.[25]

Nevertheless, SFE has some drawbacks that caused new researches to overcome them. The associated high cost of the high-pressure equipment has being considered at all times as the main drawback to SFE. However, recent studies have been established that SFE can be economically viable. For obtaining oil from grape seed, the SFE Process is economically viable in the 50 L plant, depending on the selling price of products (lower than US$ 100.00/kg).[26] Prado *et al*.[27] also studied the economic viability of SFE of oil and carotenoids from three Amazon palm trees: Buriti, pupunha and pressed palm fiber. Under the conditions studied, the prices of SFE oils were higher than selling prices of pressed oils, not because of the investment cost, but because of the raw material cost.

In addition, the economics of SFE is affected by slow kinetics of the process. Since high-pressures are normally used in SFE, mechanical stirring is difficult to be applied. The use of high-intensity ultrasound represents a potential efficient way to enhancing mass transfer process because of some mechanisms (radiation pressure, streaming, agitation, high amplitude vibrations, etc.). Thus, the application of ultrasound during SFE affects both the kinetics and the extraction yield once this is probably the unique practical way to produce agitation during SFE.[25,28-30]

Several studies have shown benefits on the SFE provided by ultrasound irradiation. Therefore, the application of ultrasound during supercritical extraction process has been proposed as a mechanism both for rate acceleration and extraction yield improvement [Table 1].

Riera *et al*.[28] firstly developed a pilot-scale ultrasound assisted CO_2 extraction of oil from almonds. The ultrasound power was promoted by a piezoelectric sandwich transducer inside the extractor. The results showed that in the end of the process the kinetics and the extraction yield enhanced by rate of 30% and 20%, respectively, when an ultrasound power of about 50 W was applied. Thereafter, other authors applied different configurations of ultrasound assisted CO_2 extraction to obtain compounds from different medicinal plants with positive results as shown in Table 1. Figure 2 shows possible configurations of UASFE. The configuration with ultrasonic probe (A) are preferred over that with ultrasonic bath (B) since the transducer is fitted externally in the ultrasonic bath there are some power attenuation as the ultrasound passes through the extractor walls. Hence, the power density inside the extractor somewhat lower than that provided by the output controller.

Ultrasound assisted pressurized liquid extraction

PLE has been successfully used for the extraction of several bioactive compounds from different plants.[37] A major advantage of PLE over conventional solvent extraction methods conducted at atmospheric pressure is that pressurized solvents remain in a liquid state well above their boiling points, allowing for

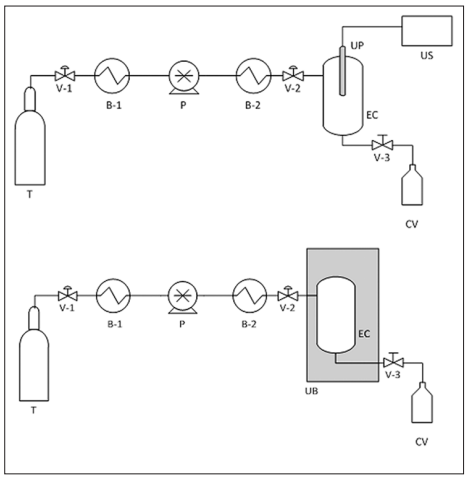

Figure 2: Possible configurations of ultrasound assisted supercritical fluid extraction (UASFE). (a) UASFE by ultrasonic probe – T: CO_2 tank; B-1: Cooling bath; B-2: Heating bath; P: Pump; EC: Extraction column; UP: Ultrasonic probe; US: Ultrasonic power supply; CV: Collector vessel; V-1, V-2, V-2: Control valves. (b) UASFE by ultrasonic bath – T: CO_2 tank; B-1: Cooling bath; B-2: Heating bath; P: Pump; EC: Extraction column; UB: Ultrasonic bath; CV: Collector vessel; V-1, V-2, V-2: Control valves

Table 1: Comparison of different benefits on the SFE provided by ultrasound irradiation for selected medicinal plants

Medicinal plant	Target compound	Experimental conditions						Results	Reference
		Quantity of raw material (kg)	Particle size	Pressure (MPa)	Temperature (°C)	Ultrasonic power (W)	Ultrasonic frequency (kHz)		
Almonds	Almond oil	1.5	3-4 and 9-10 mm	28	55	50	18	The extraction yield was increased in 20% when the SFE was ultrasonically assisted. In addition, it was observed that small particle size favor the ultrasonic action	[28]
Almonds	Almond oil	1.5	3-4 mm	20-32	45 and 60	85	18	The extraction yield reach up to 90% with SFE assisted by ultrasound	[31]
Cocoa cake	Cocoa cake oil	1.5	2-3.5 mm	32	65	85	18	The application of ultrasound increases the extraction yield by approximately 43%	
Ginger rhizomes	Pungent compounds	Not informed	4-8 mm	16	40	300	20	The recovery of pungent compounds from ginger was significantly increased under the influence of ultrasound, with improvements of up to 30% toward the end of the extraction time	[18]
Adlay seeds	Adlay oil	0.1	0.30-0.45 mm	10-30	30-55	110	20	The results showed that the extraction yield increased 14% with sonication. The operation conditions of SFE with sonication were milder	[32]
Marigold	Lutein esters	0.1	0. 198-0.245-0.350-0.833 mm	17.5-32.5	35-55	100-400	25-33	The mass transfer coefficient in the solid phase (ks) increased from 3.1×10^{-9}-4.3×10^{-9} due to ultrasound irradiation. The results showed that the yield of lutein esters increased significantly with the presence of ultrasound (P<0.05)	[33]
Ginseng	Ginsenosides	0.1	Not informed	24	45	7.6	20	The ginsenoside extraction yield from supercritical CO2 reverse microemulsion with ultrasound was 2.63-fold higher than that without ultrasound	[34]
Adlay seeds	Adlay oil	0.1	12-20-60-80 mesh	10-25	35-50	110	20	Compared with SFE, SFE assisted by ultrasound could give a 14% increase in the extraction yield with less severe operating conditions	[35]
Malagueta pepper	Oleoresin	0.02	0.177-0.342 and 1.18-1.68 mm	15	40	360	20	The extraction yield slightly increased when SFE was assisted by ultrasound. The highest increase was obtained with particles of 1.18-1.68 mm	[36]

SFE=Supercritical fluid extraction

high-temperature extraction. These conditions improve analyte solubility and the kinetics of desorption from matrices.[38]

The use of a PLE technique is an attractive alternative because it allows for fast extraction and reduced solvent consumption. PLE enables the rapid extraction (<30 min) of analytes in a closed and inert environment under high-pressures (no higher than 20 MPa) and temperatures (25-200°C). Hence, extracting solvents that are inefficient in extracting at low temperatures, may be much more efficient at the elevated temperatures used in PLE.[39]

Based on positive results obtained by coupling ultrasound with other extraction techniques, the Richter's group in Chile studied the extraction of contaminant compounds from soil using PLE coupled with ultrasound.[40,41] In the first work,[40] the authors observed that when the PLE was assisted by ultrasound, the extraction time can be reduced from 20 to 10 min obtaining quantitative recoveries of aliphatic and polycyclic aromatic hydrocarbons from soils. When UAPLE was compared with Soxhlet extraction, the results provided were statistically lower than those obtained by the conventional method. However, it is important to point that the extraction time is decreased from 20 h to <1 h and the organic solvent used in the extraction procedure can be decreased to <5% of its initial value. In other work,[41] to extraction of polychlorinated biphenyls from biosolids, the recovery of the PLE method was 73%, which was significantly improved (103%) when PLE was assisted with 30 min of ultrasound.

The experimental apparatus used to UAPLE is similar to that used for UASFE presented in Figure 2, except that the solvent no needs to be pressurized before get in the system because it is already in the liquid state. Normally, PLE employs generally recognized as safe (GRAS) solvents, such as ethanol and water.[42] However, the use of aqueous surfactant solutions as alternative solvent systems in PLE was reported for the extraction of ginsenosides from ginseng roots (*Panax quinquefolium*). When compared with the use of pure water or methanol, the presence of a common non-ionic surfactant (Triton X-100) in water at a concentration above its critical micelle concentration enhanced the amount of ginsenosides extracted. The advantages of using aqueous non-ionic surfactant solutions were also demonstrated by comparing performances between ultrasonic-assisted extraction and PLE methods. These advantages may be provided by the solubility-enhancement effect of the Triton X-100 micelles. For example, certain surfactants are known to increase the mass-transfer co-efficient during the desorption of pollutants from soil to water, presumably due to the better swelling of soil organic matters and more complete diffusion of the solvent into the solid matrix.[43]

Thompson and Doraiswamy[19] in their study have reported that the addition of surfactants to ultrasonic systems reduces the surface tension of the medium, thus reducing the cavitation threshold and facilitating the generation of bubbles. Based on these aspects, we can expect that using surfactant solutions as solvent in PLE and applying ultrasonic in this system, the results can be promising. Assuming that the addition of surfactant could act to enhance of solubility of the compounds in the extracting solvent and also could reduce the surface tension, the generation of cavitation bubbles consequently will be facilitated. These effects combined could provide good results of mass transfer in the extraction process.

Recently, glycol derived solutions, mainly polyethylene glycol (PEG) solutions have attracted increasing interest as novel solvents due their excellent properties and potential application to extraction in analytical chemistry.[44] Owing to their good biocompatibility and low immunogenicity, PEGs are on the Food and Drug Administration's (FDA's) GRAS list and have been approved by FDA for internal consumption. Among several advantages, PEG has good miscibility with water and organic solvents, as well as good solubility for various organic compounds. Therefore, PEGs are used as environmentally friendly solvents. Moreover, the addition of PEG in solutions of water or other solvents can increase the solution viscosity. PEG has been used as a green solvent in the microwave-assisted extraction of flavones and coumarin compounds from medicinal plants.[45] But to our own known, PEG solutions still were not used as extracting solvent to ultrasound-assisted extraction. As discussed previously, the ultrasonic intensity increases for solvents with high viscosity. Therefore, we can expect that the use of solutions with high viscosity as alternative solvent for ultrasound assisted extraction process can enhance the mass transfer producing good results of yield and selectivity of extraction.

Modeling of ultrasound assisted pressurized fluid extraction

The mass transfer process in solid-liquid extraction involves two chief steps. According to the model proposed by Sovová[46] in modeling SFE, as a result of seed physical manipulation such crushing the extracted solid contains both broken and intact cells. It is then assumed that micro-structurally, a seed particle contain: (i) Soluble material easily accessible, which is extracted at a rate that is controlled by the external resistance to mass transfer and is located in fractured cells in the particle surface; and (ii) "tied" soluble material, which is extracted at a rate that is determined by internal mass transfer mechanisms and is localized in undamaged cells and/or partially damaged cells in the inner portions of the particle. This second step is usually much slower and regarded as limiting step for most solid-liquid systems.

In the literature, some authors affirm that the effective enhancement of extraction with ultrasound should mainly affect the second step.[7,47] This affirmation is according with the founded by some authors,[33,36,48] however, there is no consensus regarding this point. Balachandran *et al*.[18] have reported inverse effect. They observe that when ultrasound is applied during SFE process, the predicted effective diffusivity in the first extraction step approximately doubles, suggesting that the ultrasonic vibration has either increased the number of ruptured cells and/or provided faster access for the solvent to remove solutes

from these cells. The effective diffusivity in the second stage also increases when ultrasound is applied, but the enhancement is less significant. Nevertheless, all authors agree that each solid matrix-solvent system have a particular interaction mode and then the ultrasound effect can act by different ways.

To the best of our knowledge, there is few or any work about modeling of UAPLE. However, it is an important field to study.

CONCLUSION

The aspects presented in this work established the potentiality of coupling ultrasound with high-pressure green extraction techniques to overcome its drawbacks. The major advantages of ultrasound assisted extraction are the less energy requirement, solvent usage and process time. The variables of the process have a strong influence on the extraction performance and should be careful studied in the laboratory for any process in the pharmaceutical, cosmetic or food industry to obtain bioactive compounds from medicinal plants.

ACKNOWLEDGMENTS

Renata Vardanega would like to thank CNPq (process 140282/2013-0) and FAPESP (2013/17260-5) for the doctoral fellowships. Diego T. Santos is thankful to FAPESP (processes 2010/16485-5; 2012/19304-7) for postdoctoral fellowships. M. Angela A. Meireles thanks CNPq for the productivity grant (302778/2007-1). The authors acknowledge the financial support from CNPq and FAPESP (processes 2009/17234-9; 2012/10685-8).

REFERENCES

1. Shirsath SR, Sonawane SH, Gogate PR. Intensification of extraction of natural products using ultrasonic irradiations-A review of current status. Chem Eng Process Process Intensification 2012;53:10-23.
2. Palma M, Barbero GF, Piñeiro Z, Liazid A, Barroso CG, Rostagno MA, *et al*. Extraction of natural products: Principles and fundamental aspects. In: Rostagno MA, Prado JM, editors. Natural Product Extraction: Principles and Applications. Londres: RSC Publishing; 2013. p. 58-88.
3. Pingret D, Tixier-Fabiano AS, Chemat F. Ultrasound-assisted extraction. In: Rostagno MA, Prado JM, editors. Natural Product Extraction: Principles and Applications. Londres: RSC Publishing; 2013. p. 89-112.
4. Luque-García JL, Luque de Castro MD. Ultrasound: A powerful tool for leaching. Trends Analyt Chem 2003;22:41-7.
5. Patist A, Bates D. Ultrasonic innovations in the food industry: From the laboraty to commercial production. Innov Food Sci Emerg Technol 2008;9:147-54.
6. Rostagno MA, Villares A, Guillamón E, García-Lafuente A, Martínez JA. Sample preparation for the analysis of isoflavones from soybeans and soy foods. J Chromatogr A 2009;1216:2-29.
7. Vinatoru M. An overview of the ultrasonically assisted extraction of bioactive principles from herbs. Ultrason Sonochem 2001;8:303-13.
8. Takeuchi TM, Pereira CG, Braga ME, Maróstica MR, Leal PF, Meireles MAA. Low pressure solvent extraction (solid-liquid extraction, microwave assisted, and ultrasound assisted) from condimentary plants. In: Meireles MA, editor. Extracting Bioactive Compounds for Food Products. Boca Ratun, USA: CRC Press/Taylor and Francis Group; 2009. p. 137-2189.
9. Wang L, Weller CL. Recent advances in extraction of nutraceuticals from plants. Trends Food Sci Technol 2006;17:300-12.
10. Vinatoru M, Toma M, Radu O, Filip PI, Lazurca D, Mason TJ. The use of ultrasound for the extraction of bioactive principles from plant materials. Ultrason Sonochem 1997;4:135-9.
11. Escaplez MD, García-Pérez JV, Mulet A, Cárcel JA. Ultrasound-assisted extraction of natural products. Food Eng Rev 2011;3:108-20.
12. Soria AC, Villamiel M. Effect of ultrasound on the technological properties and bioactivity of food: A review. Trends Food Sci Technol 2010;21:323-31.
13. Mulet A, Cárcel JA, Benetido J, Sanjuan N. Application of low-intensity ultrasonics in dairy industry. In: Engineering and Food for the 21st Century. Boca Raton, FL: CRC Press; 2002. p. e-book.
14. Berlan J, Trabelsi F, Delmas H, Wilhelm AM, Petrignani JF. Oxidative degradation of phenol in aqueous media using ultrasound. Ultrason Sonochem 1994;1:S97-102.
15. Hilgenfeldt S, Brenner MP, Grossmann S, Lohse D. Analysis of Rayleigh-plesset dynamics for sonoluminescing bubbles. J Fluid Mechanics 1998;365:171-204.
16. Kemmere M, Kuijpers M, Jacobs L, Keurentjes J. Ultrasound-induced polymerization of methyl methacrylate in liquid carbon dioxide: A clean and safe route to produce polymers with controlled molecular weight. Macromol Symp 2004;206:321-31.
17. Kuijpers MW, van Eck D, Kemmere MF, Keurentjes JT. Cavitation-induced reactions in high-pressure carbon dioxide. Science 2002;298:1969-71.
18. Balachandran S, Kentish SE, Mawson R, Ashokkumar M. Ultrasonic enhancement of the supercritical extraction from ginger. Ultrason Sonochem 2006;13:471-9.
19. Thompson LH, Doraiswamy LK. Sonochemistry: Science and engineering. Ind Eng Chem Res 1999;38:1215-49.
20. Adewuyi YG. Sonochesmistry: Environmental science and engineering applications. Ind Eng Chem Res 2001;40:4681-715.
21. Fischer CH, Hart EJ, Henglein AJ. Hydrogen/deuterium isotrope exchange in the hydrogen deuteride-water system under the influence of ultrasound. J Phys Chem 1986;90:3059-60.
22. Seghal C, Yu TJ, Sutherland RG, Verrall R. Use of 2,2-diphenyl-1-picrylhydrazyl to investigate the chemical behavior of free radicals induced by ultrasonic cavitation. J Phys Chem 1982;86:2982-6.
23. Ince NH, Tezeanli G, Belen RK, Apikyan PG. Ultrasound as a catalyzer of aqueous reaction systems: the state of the art and environmentak applications. Appl Catal B 2001;29:167-76.
24. Leal PF, Kfouri MB, Alexandre FC, Fagundes FH, Prado JM, Toyama MH, *et al*. Brazilian Ginseng extraction via LPSE and SFE: Global yields, extraction kinetics, chemical composition and antioxidant activity. J Supercrit Fluids 2010;54:38-45.
25. Riera E, Blanco A, García J, Benedito J, Mulet A, Gallego-Juárez JA, *et al*. High-power ultrasonic system for the enhancement of mass transfer in supercritical CO_2 extraction process. Phys Procedia 2010;2:141-6.
26. Prado JM, Dalmolin I, Carareto ND, Basso RC, Meirelles AJ, Oliveira JV, *et al*. Supercritical fluid extraction of grape seed: Process scale-up, extract chemical composition and economical evaluation. J Food Eng 2012;109:249-57.

27. Prado JM, Assis AR, Maróstica-Júnior MR, Meireles MA. Manufacturing cost of supercritical-extracted oils and carotenoids from amazonian plants. J Food Process Eng 2010;33:348-69.
28. Riera E, Golás Y, Blanco A, Gallego JA, Blasco M, Mulet A. Mass transfer enhancement in supercritical fluids extraction by means of power ultrasound. Ultrason Sonochem 2004;11:241-4.
29. Cárcel JA, García-Pérez JV, Benetido J, Mulet A. Food process innovation through new technologies: use of ultrasound. J Food Eng 2012;110:200-7.
30. Seidi S, Yamini Y. Analytical sonochemistry: developments, applications, and hyphenations of ultrasound in sample preparation and analytical techniques. Cent Eur J Chem 2012;10:938-76.
31. Riera E, Blanco A, García J, Benedito J, Mulet A, Gallego-Juárez JA, *et al*. High-power ultrasonic system for the enhancement of mass transfer in supercritical CO2 extraction processes. Ultrasonics 2010;50:306-9.
32. Hu AJ, Zhao S, Liang H, Qiu TQ, Chen G. Ultrasound assisted supercritical fluid extraction of oil and coixenolide from adlay seed. Ultrason Sonochem 2007;14:219-24.
33. Gao Y, Nagy B, Liu X, Simándi B, Wang Q. Supercritical CO_2 extraction of lutein esters from marigold (*Tagetes erecta* L.) enhanced by ultrasound. J Supercrit Fluids 2009;49:345-50.
34. Luo D, Qiu T, Lu Q. Ultrasound-assisted extraction of ginsenosides in supercritical CO_2 reverse microemulsions. J Sci Food Agric 2007;87:431-6.
35. Hu A, Zhang Z, Zheng J, Wang Y, Chen Y, Liu R, *et al*. Optimizations and comparison of two supercritical extractions of adlay oil. Innov Food Sci Technol 2012;13:128-33.
36. Santos P, Aguiar AC, Rezende CA, Martínez J. Supercritical carbon dioxide extraction of oleoresin from malagueta pepper (*Capsicum frutescens* L.) enhanced by ultrasound, in III Iberoamerican Conference of Supercritical Fluids, Cartagena de Indias, Colombia, 2013. p. 1-7.
37. Petersson EV, Liu J, Sjöberg PJ, Danielsson R, Turner C. Pressurized hot water extraction of anthocyanins from red onion: A study on extraction and degradation rates. Anal Chim Acta 2010;663:27-32.
38. Richter BE, Jones BA, Ezzell JL, Porter NL. Accelerated solvent extraction: a tehcnique for sample preparation. Anal Chem 1996;68:1033-9.
39. Ju ZY, Howard LR. Effects of solvent and temperature on pressurized liquid extraction of anthocyanins and total phenolics from dried red grape skin. J Agric Food Chem 2003;51:5207-13.
40. Richter P, Jiménez M, Salazar R, Maricán A. Ultrasound-assisted pressurized solvent extraction for aliphatic and polycyclic aromatic hydrocarbons from soils. J Chromatogr A 2006;1132:15-20.
41. Rocco G, Toledo C, Ahumada I, Sepúlveda B, Cañete A, Richter P. Determination of polychlorinated biphenyls in biosolids using continuous ultrasound-assisted pressurized solvent extraction and gas chromatography-mass spectrometry. J Chromatogr A 2008;1193:32-6.
42. Santos DT, Albuquerque CL, Meireles MA. Antioxidant dye and pigment extraction using homemade pressurized solvent extracion system. Procedia Food Sci 2011;1:1581-8.
43. Choi MP, Chan KK, Leung HW, Huie CW. Pressurized liquid extraction of active ingredients (ginsenosides) from medicinal plants using non-ionic surfactant solutions. J Chromatogr A 2003;983:153-62.
44. Chen J, Spear SK, Huddleston JG, Rogers RD. Polyethylene glycol and solutions of polyethylene glycol as green reaction media. Green Chem 2005;7:64-82.
45. Zhou T, Xiao X, Li G, Cai ZW. Study of polyethylene glycol as a green solvent in the microwave-assisted extraction of flavone and coumarin compounds from medicinal plants. J Chromatogr A 2011;1218:3608-15.
46. Sovová H. Rate of vegetable oil extraction with supercritical CO_2. Modeling of extraction curves. Chem Eng Sci 1994;49:409-14.
47. Toma M, Vinatoru M, Paniwnyk L, Mason TJ. Investigation of the effects of ultrasound on vegetal tissues during solvent extraction. Ultrason Sonochem 2001;8:137-42.
48. Riera E, Golás Y, Blanco A, Gallego JA, García-Reverter J, Subirats S. Effect of high-intensity ultrasound on the particulate almonds oil extraction kinetics using supercritical CO_2. In: 6th International Symposium on Supercritical Fluids, Versailles, France, 2003. p. 1-6.

How to cite this Article: Vardanega R, Santos DT, Meireles MAA. Intensification of bioactive compounds extraction from medicinal plants using ultrasonic irradiation. Phcog Rev 2014;8:88-95.

Source of Support: This work had financial support from FAPESP and CNPq. Renata Vardanega would like to thank CNPq (process 140282/2013-0) and FAPESP (2013/17260-5) for the doctoral fellowships. Diego T. Santos is thankful to FAPESP (processes 2010/16485-5; 2012/19304-7) for postdoctoral fellowships. M. Angela A. Meireles thanks CNPq for the productivity grant (302778/2007-1). The authors acknowledge the financial support from CNPq and FAPESP (processes 2009/17234-9; 2012/10685-8), **Conflict of Interest:** None declared