Food Engineering Reviews
https://doi.org/10.1007/s12393-025-09425-6

A Comprehensive Review of the Development of Green Extraction Methods and Encapsulation of Theobromine from Cocoa Bean Shells for Nutraceutical Applications

Erick Alvarez-Yanamango[1,4] · **Daniel Obregon**[2,4] · **Alfredo Ibañez**[3,4]

Received: 17 February 2025 / Accepted: 28 July 2025

Abstract
Cocoa bean shells (CBS) represent up to 20% of the waste from roasted beans in emerging countries, such as Peru, one of the leading producers of fine-aroma cocoa (*Theobroma cacao L.*) in the world. Due to the high phenolic and theobromine concentrations in agricultural residues such as cocoa bean shells (CBS), multidisciplinary research is focused on optimizing the extraction, characterization, and evaluation of phenolic compounds present in CBS. To provide a complete guide for the extraction of theobromine from CBS, we present here the main methods of extraction and stabilization (encapsulation) of theobromine present in CBS, moving from conventional techniques to others considered "green," such as ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), supercritical fluid extraction (SFE), pressurized liquid extraction (PLE), even deep eutectic solvent extraction (DES), hydrodynamic cavitation reactors (HCR), pulsed electric field (PEF), and high-voltage electric discharge extraction (HVED), pressurized hot water extraction (PHWE) and subcritical water extraction (SCE), among others. Here, the significant increase in theobromine concentration of the extracts is highlighted, as well as the importance of microencapsulation and nanoencapsulation in protecting their bioactivity. The UAE and MAE methods are more effective for theobromine extraction, respectively. On the other hand, encapsulations have been evaluated primarily with maltodextrin mixed with gum Arabic, chitosan, and whey protein by spray drying or freeze-drying. It is concluded that obtaining a nutraceutical product from CBS in a sustainable circular agricultural economy requires optimizing scalable green extraction processes, such as US, and exploring new encapsulated materials and their mixtures to stabilize bioactive compounds, taking advantage of synergistic protection effects.

Keywords *Theobroma cacao L.* · Cocoa bean shell · Nutraceutical · Theobromine · Green extraction methods · Encapsulation

Introduction

Emerging agricultural residues, for example, from the chocolate industry, contribute to a circular economy by providing low-cost and sustainable renewable (bio)resources for nutraceutical production. Nutraceuticals, a functional food with high concentrations of bioactive compounds, have become a multibillion-dollar industry [18].

Cocoa (*Theobroma cacao L.)* is a crop whose origin, domestication, and use originated in South America [69]. Its leading producers are African countries (Ivory Coast and Ghana) and South American countries, such as Ecuador and Brazil. Peru is one of the leading producers and a major global exporter of fine-flavor cocoa, with the Netherlands, Indonesia, Mexico, Malaysia, and the USA being its primary markets [56].

✉ Erick Alvarez-Yanamango
erick.alvarez@pucp.edu.pe

1 Engineering Department, Pontificia Universidad Católica del Perú, San Miguel, Lima, Peru

2 Sciences Department, Chemistry Section, Pontificia Universidad Católica del Perú, San Miguel, Lima, Peru

3 Institute for Omics Sciences and Applied Biotechnology (ICOBA PUCP), Pontificia Universidad Católica del Perú, San Miguel, Lima, Peru

4 Agro-Industrial Technologies and Processes Research Group (ITEPA PUCP), Pontificia Universidad Católica del Perú, San Miguel, Lima, Peru

Published online: 23 August 2025

In Peru, cocoa production involves 90,000 producers, mainly family farmers, in 16 of Peru's 24 regions. San Martin, Junin, Ucayali, Huanuco, and Cusco are the five prominent producing regions, accounting for 86% of total national production [82].

In 2022/2023, the worldwide production of cocoa beans was estimated to be around 4.9 million tons [56], of which the by-products (cocoa husk, cocoa shell, and pulp) correspond to 85% of the cocoa production [15]. In Peru, in the same year (2023), the total production of dried beans was approximately 170,300 tons [82]. Interestingly, during the processing of cocoa beans, since the harvesting of cocoa, the cocoa industry produces waste by-products with valuable health properties, which represent between 10 and 20% of the CBS [49, 110, 111] Based on available data, it was estimated that in Peru, cocoa bean shells (CBS) production reached between 17 000 and 34 000 tons in 2023.

Furthermore, cocoa waste by-products, i.e., cocoa pod husks (CPH) and cocoa bean shells (CBS), have been evaluated due to the presence of different bioactive compounds such as methylxanthines (theobromine and caffeine), polyphenols (protocatechuic acid, procyanidin B2, catechin, and epicatechin), and phytosterols (campesterol, stigmasterol, β-sitosterol) [15, 35, 49, 110]. Meanwhile, polyphenols – one of the main compounds found in CBS and CPH [35] – serve as an antioxidant that prevents the progression of many diseases. Theobromine – another main compound present in the CBS – is becoming more relevant due to its [49] properties as a nutraceutical.

Theobromine is an antioxidant and anti-inflammatory that has been shown to positively influence cardiovascular health and brain function positively [40], act as an anticarcinogenic agent [126], diminish obesity and diabetes disorders [59], improve fertility, and reduce neurological and neurodegenerative disorders such as Alzheimer's and Parkinson's disease [44, 60]. Furthermore, theobromine is being proposed as a new medical treatment for lithiasis, i.e., kidney stone formation. [26, 29, 52].

Polyphenols and theobromine could be extracted from CPH and CBS using various technologies, such as ohmic heating [110], hydrodynamic cavitation extraction [46], pulsed electric field [9, 17], supercritical CO_2 [41, 51, 80] with ethane [83], ultrasonic assisted [95], supercritical water extraction [63, 64], pressured hot water extraction [89], and microwave extraction [32, 43].

Previous literature has shown that new technologies, considered “green processes,” are being highlighted in bioactive recovery from CBS to follow circular economy principles, i.e., utilizing agricultural residues and clean processes. Furthermore, the focus of all extraction processes showcased in the literature is mainly on optimizing the recovery of phenolic compounds and demonstrating their antioxidant activity. For this reason, this review aims to analyze different techniques and technologies that allow the extraction and optimized stabilization of other components present in CBS, such as methylxanthines, in particular theobromine, since it shows nutraceutical properties for the prevention and treatment of diseases, having enormous possibilities to be incorporated in food, cosmetic, or even pharmaceutical formulations.

Methods and Literature Search

For this review, peer-reviewed scientific literature published between 2000 and 2024 was analyzed. However, some previous studies were incorporated due to their relevance to the field or because they represent the most current research available on specific aspects of the topic. The bibliographic search was conducted primarily through specialized databases and search engines, including Scopus, Web of Science, ResearchGate, Google Scholar, MDPI, PubMed, and SciELO. Additional sources were identified through a manual review of the references cited in the selected articles. Various search terms were used, both individually and in combination, including keywords such as"polyphenols,""theobromine,""functional,""cocoa,""Theobroma,""byproduct,"and"cocoa bean shell,"among other related terms.

Generation of Cocoa Bean Shell (CBS) as a by-product of Post-Harvest Processing

Cocoa (Theobroma cacao L.) undergoes several harvesting processes to obtain products such as butter, liquor, and cocoa powder, generating by-products with a high content of great commercial value. The latter includes mucilage (8–10% of the fresh fruit), pod husk (CPH, 65–80% of the fresh fruit), and bean husk (CBS, 10–20% of bean weight) [49, 110, 111]

Figure 1 illustrates the operational sequence for obtaining cocoa bean husk (CBS). In the first stage, the seeds undergo a fermentation process that lasts 5 to 7 days, generating the precursors of the characteristic aroma and flavor of cocoa. Subsequently, the beans are dried, either in the sun or in mechanical dryers, to reduce the humidity to below 8%, which prevents microbial proliferation and improves the conservation of the bean.

The dried beans are then roasted at temperatures above 100 °C, a process that not only intensifies the volatile compounds and the sensory profile of the cocoa but also weakens the bond between the husk and the cotyledon. This structural modification enables the shelling process to be carried out through friction and mechanical agitation, resulting in the CBS as a by-product.

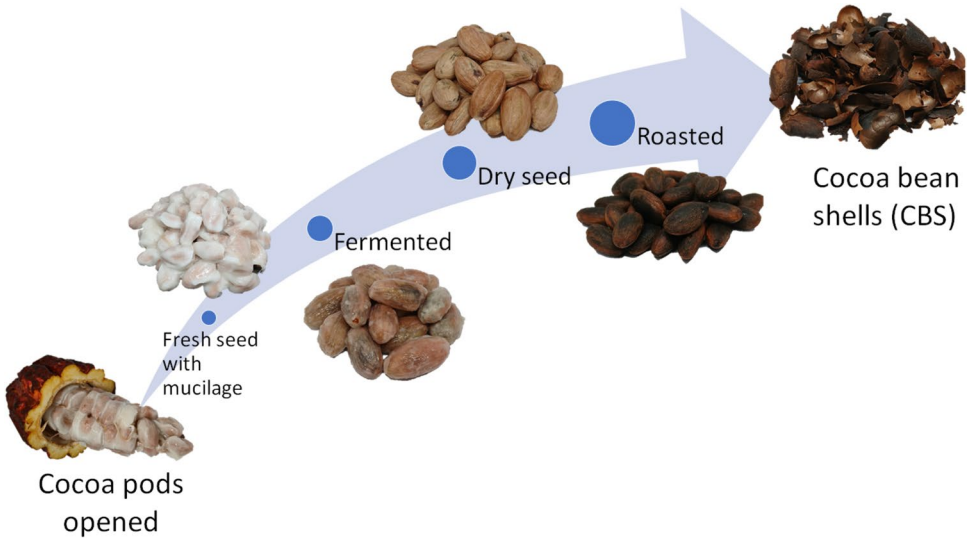

Fig. 1 Steps to obtain cocoa bean shell (CSB) residues

The Extraction Process and Quantification of Theobromine from Cocoa Bean Shell

In the process of extracting theobromine from cocoa bean shells (CBS), researchers have focused on both fermented and unfermented, as well as roasted and unroasted, cocoa beans, all of which are reduced in size to less than 500 µm. Once pulverized to this particle size to access the CBS metabolites, the bioactive compounds in CBS can be extracted using conventional and non-conventional methods. The conventional methods are simple, readily available, and cost-effective; however, their effectiveness is limited by the solvents'ability to penetrate plant cell walls and their potential toxicity.

Traditionally, CBS extracts have been inspected with ultraviolet–visible spectroscopy (UV–Vis). UV–Vis spectroscopy can estimate the total content of phenolic compounds and methylxanthines after extraction and its subsequent cleaning step to eliminate interferences, such as polyphenols and proteins [95]. The latter is possible through Carrez clarification method, which involves the addition of a solution of potassium ferrocyanide and zinc acetate or zinc sulfate [22]. These forms insoluble precipitates of proteins and colloidal substances that can be separated by centrifugation or filtration, thereby helping to clarify the sample before bioactive analysis. [79]. However, more precise and accurate analytical techniques are now being used to identify and quantify methylxanthines present in CBS extracts. The most common is high-performance liquid chromatography (HPLC) coupled to different detectors, such as a diode array detector (DAD) [14, 46, 94]. [119],), and electrospray ionization of a tandem mass spectrometry system (ESI–MS/MS)[8, 50, 96]. These analytical techniques for methylxanthine identification and quantification have been further improved by using ultra-high-performance liquid chromatography (UPLC or UHPLC).

Conventional Solid–Liquid Extraction

Conventional extraction techniques of methylxanthines from CBS are based on solid–liquid extraction, such as decoction (boiling infusion), leaching, maceration, and percolation [101].

The extraction principle is based on the transfer of the compound present in the solid to the mass of the solvent, where five mass transfer steps are usually involved: penetration of the solvent into the surface of the solid, diffusion through the solid, solubilization of the compound in the solvent, diffusion to the surface of the solid, and finally, external transfer to the total solution. Therefore, extraction depends on how fast the compound dissolves and reaches equilibrium in the liquid [77, 97]. Furthermore, the overall temperature (T_{bulk}) of the system and the type of solvent are known to have a significant impact on the mass transfer processes. Thus, diffusion rates would increase with an increase in the local temperature of the solute (local T), thereby reducing the extraction time [77]. In particular, water, ethanol, methanol, or their combination has been traditionally selected for theobromine extraction from CBS. Moreover, the binary mixture (water: ethanol) is the most commonly used due to its compatibility with food preparation (i.e., water and ethanol are green solvents)[98]. In many cases, solid–liquid extraction requires either mechanical or magnetic agitation to enhance the extraction process. On the contrary, maceration is a static solid–liquid extraction process that does not need agitation. Unfortunately, maceration requires a longer extraction time than other solid–liquid systems to maximize the recovery of methylxanthines.

Regardless of the solid–liquid extraction system used, water requires a higher temperature during extraction than ethanol or methanol to improve the solubility and diffusion coefficient of phenolic compounds, with the disadvantage of thermal degradation and lower extraction selectivity of compounds [21, 101]. Therefore, to prevent the thermal destruction of metabolites during maceration, where longer extraction times are used, alternative solvents, such as water or binary phases with similar polarity and solubility, are preferred [98, 115]. Table 1 below presents recent applications of conventional extraction techniques. The fermentation and roasting that the cocoa bean undergoes influence the theobromine recovery efficiency of the CBS as much as the extraction parameters. The particle size of the CBS (< 300 µm), the agitation, and the type of solvent have a significant influence on the theobromine extraction time and yield. The use of ethanol in a stirred system requires a shorter extraction time of 20 min compared to maceration, which can take up to 720 min. Additionally, the use of ethanol requires lower temperatures than water as a solvent (> 80 °C) to enhance theobromine recovery. Therefore, ethanol stands out for its theobromine recovery efficiency due to its low energy cost and its consideration as a green solvent in conventional extraction techniques.

Microwave-Assisted Extraction

Microwave radiation is a fast and efficient, environmentally friendly process that reduces extraction time and solvent requirements, increasing yields and improving purity compared to conventional heating methods [70, 74]. Microwave-assisted extraction (MAE) significantly enhances mass transfer from biomass to solvent by a temperature-induced diffusion (TID). Unlike conventional isothermal processes, where solute transport depends mainly on concentration gradients, MAE also involves thermal gradients that modify the internal chemical potential of the biomass [113]. This phenomenon results in increased water absorption in cells, which can lead to elevated internal pressures that weaken or even rupture cell walls [77]. As a result, the release of bioactive compounds from the biomass is facilitated, increasing the extraction yield and reducing the process time. In addition, microwave heating produces a localized increase in temperature (local T) higher than the average temperature of the system (Tbulk), which accelerates the solubilization of compounds and improves the yield [77]. This rapid heating, driven by changes in applied power, promotes cell rupture and effective diffusion of solutes into the solvent. However, this technology also has limitations. Although it reduces

Table 1 Theobromine extraction parameters by conventional extraction

CBS	Ratio L/S (mL g^{-1})	Time (min)	Temp (ºC)	Solvent concentration	Stirring	Concentration (mg g^{-1})	Reference
Ground	100	5	80	H_2O (100%)	Yes	13.2 $^{+++}$	[95]
Unroasted (100 µm)	8.55	20	Room	EtOH (63%)	Yes	Identification**	[25]
	14.28						
	20						
Fermented unroasted (250 µm)	N.I/20	720	Room	EtOH (96%)	No, maceration	7.1–9.6 ***	[35]
Fermented roasted (250 µm)						15.4—22.5 ***	
(300 µm)	500	118	25	EtOH (39.15%)	Rotary agitation (60 rpm)	4.7—10.6 **	[9]
Ground and defatted	20	45	Room	Water (nano pure)	Yes	9.0 ****	[55]
			55			10.3****	[55]
(500 µm)	5	60	60	EtOH 70% (v/v)	Magnetic stirring	7.40*	[107]
Ground (300 µm)	50	60–90	N.I	Water	Magnetic stirring	2.96–2.99*	[65]
(250 µm)	*20*	120	*25*	EtOH/H_2O *50:50 (v/v)*	Rotatory oscillation	4.6—9.9 $^{+}$	[8]
Unmilled	66.6	15	N.I	H_2O	Magnetic stirring	2.3 *	[11]
	33.3	45				2.9 *	
(250 µm)	20	120	25	EtOH/H_2O (50:50, v/v)	Rotatory oscillation	7.6–9.0 **	[105]
Non-fermented and unroasted (0.5 µm)	3	60	70	MeOH/H_2O 80:20 (*v/v*) Acidified pH 3	Yes	3.9 $^{++}$	[50]
Fermented and unroasted (0.5 µm)						12.0 $^{++}$	

* HPLC–DAD; ** RP-UHPLC-DAD; *** HPLC ****UHPLC; + HPLC–DAD-ESI–MS/MS; + + HPLC–MS; + + + UV–Vis (273 nm)

extraction times, prolonged exposure of the compound to elevated temperatures within the system can induce its degradation, especially if it remains in contact with the biomass for an extended period. [77]. Additionally, the drastic temperature change caused significant damage to the structural plant wall and solubilized unwanted compounds, requiring more complex purification steps and thereby increasing overall process costs. As a result, selective heating of molecules efficiently provides the energy needed to overcome the activation barrier; however, careful control of operating parameters is required to avoid the co-extraction of unwanted compounds and degradation of the bioactive compounds of interest. Microwave-assisted extraction of bioactive compounds from CBS is shown in Fig. 2.

Table 2 below presents recent applications of microwave-assisted extraction of methylxanthines from CBS, along with their process factors. Microwave-assisted extraction (MAE) enhances the extraction efficiency of theobromine from cocoa peel by up to 72% and caffeine from cocoa seeds by up to 150% without altering the extracts. The extraction mix consisted of 0.5 g of sample, 90 mL of distilled water, and 5 mL of Carrez I reagent, and was performed using 210 W and an irradiation time of 5 min [43].

Darasia et al. [32] placed a mixture of cocoa pod husk powder and ethanol in an Erlenmeyer flask, which was subjected to microwave heating at 180 W for 3 min. Then, the extraction was filtered, dried (rotary vacuum evaporator, 50 °C, 100 bars, 65 rpm), and stored at low temperature. This MAE extraction protocol produced the highest total phenol content of 6.473 mg GAE/g with antioxidant activity of 27.2 µg mL^{-1} compared to the traditional Soxhlet extraction [32].

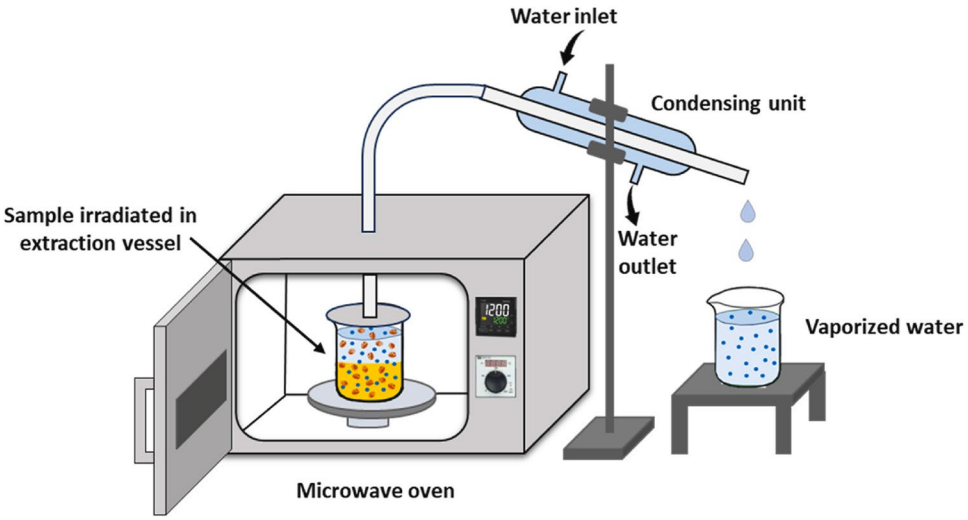

Fig. 2 Schematic representation of microwave-assisted extraction of bioactive compounds from CBS and its process factors. Reprinted from *Heliyon,* 10(10), Nayak et al. Advances in the novel and green-assisted techniques for extraction of bioactive compounds from millets: A comprehensive review, Vol. 9., Copyright 2024 with permission from Elsevier [84]

Table 2 Theobromine extraction parameters by microwave-assisted extraction

Raw material	Solvent	Ratio L/S (mL g^{-1})	Specifications	Concentration (mg g^{-1})	Reference
CBS (ground)	H_2O/DES (49%/choline chloride: oxalic acid, 1:1 mol ratio)	20	Power: 600-800W Time: 11.41 min Temperature: 35.1 ºC	4.5*	[93]
CBS ground (< 1 mm)	H_2O	25	Power: 500 W Time: 5 min Stirring: 400 rpm Temperature: 97 °C pH: 2	5.1**	[81]
			pH: 7 (phosphate buffer)	6.4 **	
			pH: 12	7.6 **	
CBS unroasted (100 µm)	EtOH/H_2O (63% v/v)	69.71	Power: 399,88 W Time: 3.6 min	Identify***	[25]
CBS ground	H_2O (with Carrez reagent)	180	Power: 210 W Time: 5 min	12.60^{+}	[43]

*HPLC–DAD; **HPLC–UV/VIS; ***RP-UHPLC-DAD; + UV–Vis (275.9 nm)

Cavitation Extraction Techniques

In general terms, cavitation extraction is a physical phenomenon involving the formation and collapse of cavities, either vapor or gas bubbles, in the solvent, which can be induced by various mechanisms. For bioactive extraction, these mechanisms can include acoustic cavitation, which is the principle of ultrasonic-assisted extraction (UAE), or hydrodynamic cavitation (HC).

Hydrodynamic cavitation occurs when the pressure in turbulent flow systems, such as those found in Venturi valves, rotors, or high-speed centrifugal pumps, abruptly reduces. [128]. This generates the formation or collapse of cavities (bubbles) in a liquid medium, producing a hot spot and shock waves that disrupt cell membranes, thereby enhancing mass transfer [28]. On its side, ultrasound-assisted extraction (UAE) is based on the controlled induction of acoustic cavitation by the application of high-frequency ultrasonic waves, ranging from 16 to 100 kHz (I = 10–1000 W/cm^2), generated by an ultrasonic transducer [108]. These waves induce the formation, growth, and implosive collapse of microbubbles in the solvent, especially in the vicinity of the biomass. This collapse produces localized pressure gradients. as well as microjets and shock waves that generate various intense mechanical and thermal effects, such as surface detachment, erosion, and fragmentation of particles, disruption of cell structures, and increased cell wall permeability, which together promote mass transfer between the biomass and the solvent [27, 116]. In addition, the bubble implosion produces macroturbulences and micromixers that contribute to the homogenization of the system and a more efficient extraction. [27].

In summary, HC does not require ultrasonic waves, but rather hydraulic mechanical energy, making it more energy-efficient and economically viable, and thus more easily scalable to an industrial level. Table 3 presents different extraction techniques for producing cavitation for theobromine extraction.

Hydrodynamic Cavitation Reactors (HCR)

Finally, a third method for producing hydrodynamic cavitation is based on mechanical forces that occur in hydrodynamic cavitation reactors (HCR) with or without moving parts, such as the venturi-type and rotor–stator HCRs (Table 3).

Hydrodynamic cavitation extraction techniques were successfully implemented in a pilot-scale plant by [46]. The authors demonstrated that HCR overcomes ultrasound and conventional extraction methods. Biomass destruction is enhanced faster due to the high-energy environment provided by the hydrodynamic cavitation technique [46]. Pilot scale tests were performed in a 25 L rotor/stator HCR in a hydroalcoholic mixture (70:30 EtOH/H_2O) at room temperature at 3000 rpm for 11 min for 47.7 cycles (each 5 s) and a total residence time of 3.93 min for theobromine extraction, compared to ultrasound-assisted extraction. Extraction by hydrodynamic cavitation yielded 14.8 vs. 9.6% w/w for ultrasound-assisted extraction. These results were improved using a ternary mixture of Hex/EtOH/H_2O (30:49:21) using cocoa shells with(without) milled. A 50% higher extraction per concentration was obtained using hydrodynamic cavitation than ultrasound-assisted extraction (UAE). Extraction ranged from 34.4 vs. 23.2 mg g^{-1} of shells for UAE to 141.6 vs. 95.5 for HCR using cocoa shells with(without) milled [46]. The intensification of the process shown by HCR over the UAE was confirmed.

Ultrasound-Assisted Extraction (UAE)

One method of achieving cavitation extraction is the use of ultrasound. In ultrasound, a high sound frequency is applied, causing rapid changes in liquid pressure. Upon decompression, a cavitation bubble rapidly collapses, producing microjets and shockwaves that can damage cell walls, increase the surface area exposed to the solvent, and enhance the release of bioactive compounds [24].

In more detail, the ultrasound-assisted extraction is based on ultrasound implosions that generate an estimated local temperature zone of around 2,000–5,000 K and pressures over 100 MPa [66, 67]. This type of cavitation extraction can be applied directly or indirectly using a sonication device with a probe or an ultrasonic bath, respectively (Fig. 3). On the one hand, the probe sonication device emits an ultrasonic wave directly into the liquid medium, producing intense cavitation in a localized area. In an ultrasonic bath, the transducers are attached to the bottom or sides of the tank, vibrating and creating cavitation bubbles in the liquid. However, they generate less intense implosions due to the indirect and diffuse nature of ultrasonic wave propagation through the liquid in the tank. [75, 100]. Although ultrasonic implosions are uniform in the bath, achieving mass transfer through acoustic agitation and micromixing, it is recommended to include mechanical agitation to ensure the efficient transmission of ultrasonic energy to the biomass, thereby achieving uniform cavitation distribution [100]. In contrast, in direct sonication, the ultrasonic transducer probe is immersed directly into the sample to create high-intensity mechanical vibrations, generating acoustic power almost 100 times higher than that of the ultrasonic bath [75]. At the yield level, direct probe sonication produces higher pressure and temperature gradients at the microscopic level ($T_{local} > T_{bulk}$), facilitating cell rupture, depolymerization of structures, and more efficient intensified mass transfer by direct mechanical disruption, providing better particle dispersion compared to bath sonication by reducing particle size distribution, resulting in higher

Table 3 Theobromine extraction parameters by ultrasound (probe and bath) and hydrodynamic cavitation extraction

Equipment		Extraction conditions						Theobromine concentration (mg g^{-1})	Reference
Device	Frequency (kHz)	Raw material	Solvent (concentration)	Ratio L/S (mL g^{-1})	Temp (°C)	Power (W)	Time (min)		
Ultrasound probe	30	CBS	EtOH/H_2O (60:40)	10	-	100	30	0.31–0.33 *	[14]
	19.9	CBS	Hex/EtOH/H_2O (30:49:21)	10	40	150	15	7.0 hydroalcoholic phase*	[46]
		CBS ground	Hex/EtOH/H_2O (30:49:21)					4.8 hydroalcoholic phase*	
		CBS (< 1000 µm)	Hex/EtOH/H_2O (30:49:21)					17.8 hydroalcoholic phase*	
	20	Cocoa peel	H_2O	100	80	240	3	15.1 ****	[95]
	20	CBS ground < 5 mm	EtOH/H_2O (70:30)	5	-	200	3	5.5 *	[107]
Ultrasound (bath)	40	CBS ground defatted	H_2O (nanopore)	20 (diluted to 25 mL for analysis)	45–75	-	45	10.1–10.6 ***	[55]
					55	-	25–65	10.1–10.3 ***	
	37	CBS	H_2O	50	40	-	60	5.9 *	[94]
	35	CBS (ground)	H_2O	N.I	60	-	30	4.9 *	[58]
			EtOH/H_2O (50:50)					2.5 *	
			EtOH/H_2O (75:25)					0.5 *	
		CBS (ground)	MeOH/H_2O/HCOOH (70:30:0,1%; v/v/v)	16.6 (diluted to 25 mL for analysis)	N.I		5/10 min (4 cycles)	9.3–12.9 *	[73]
Pulsed electric field (PEF)	50	CBS (0.3 mm)	EtOH (39%)	140 (diluted to 50 mL)		PEF intensity: 1.74 kV cm^{-1} Post-PEF extraction: 118.54 min Current: 100 A	11.99 µs Pulses: 991.28	4.6–10.9 ++	[9]
High-voltage electric discharge extraction (HVED)	100	CBS ground (< 0.3 mm)	H_2O	50		Current: 10 A Voltage: 12 kV	60 min	6.0 *	[65]
				30		Current: 10 A Voltage: 30 kV	30 min	5.3 *	
	40	CBS (ground)	H_2O	66.6		Voltage: 30 kV	15 min	3.0 *	[11]
	80			33.3				3.3 *	
Hydrodynamic cavitation reactor (HCR, 47 cycles of 5 s)		CBS	EtOH/H_2O (70:30)	10	Room (Stir: 3000 rpm)		11	13.5 hydroalcoholic phase*	[46]
		CBS (< 1000 µm)	Hex/EtOH/H_2O (30:49:21)					32.7 hydroalcoholic phase*	

*HPLC–DAD; **UPLC; *** UHPLC, **** UV–Vis; ++ RP-HPLC–PDA

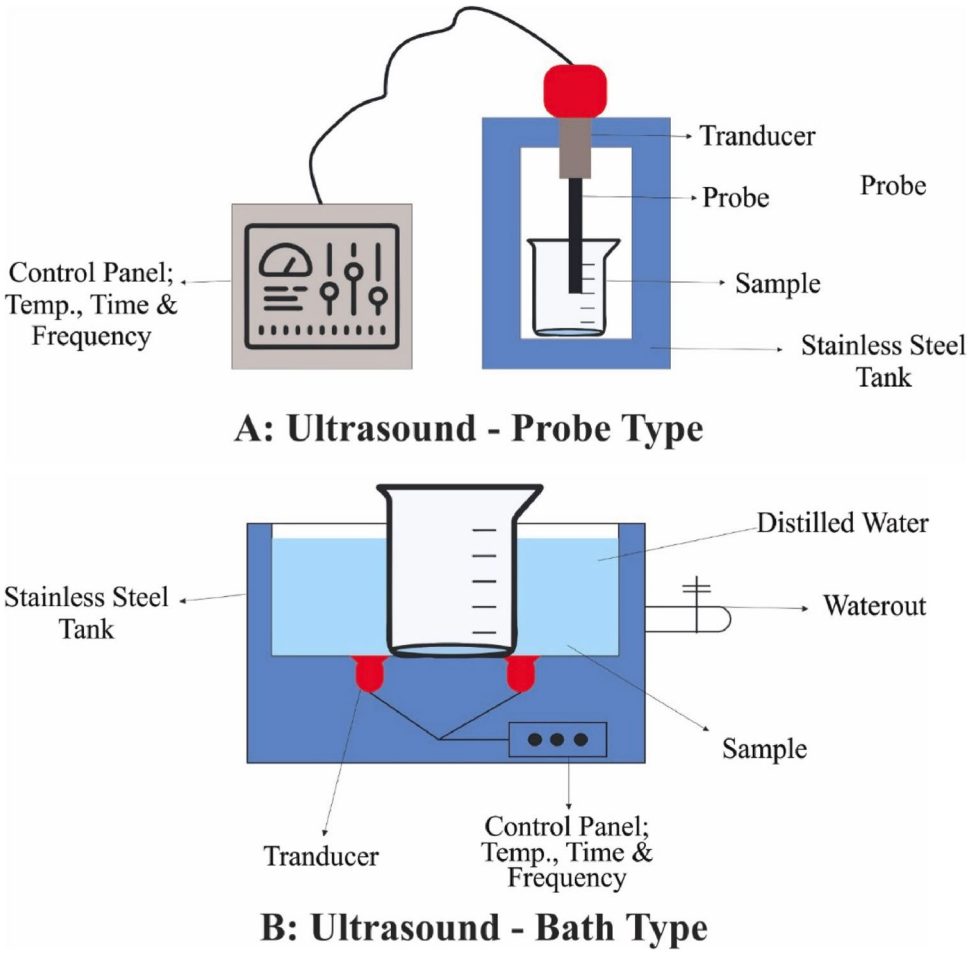

Fig. 3 Schematic representation of the ultrasonication extraction of bioactive compounds from CBS and its process factors. Reprinted from *Journal of Agriculture and Food Research*, Vol 14, Roobab et al. An updated overview of ultrasound-based interventions on bioactive compounds and quality of fruit juices, 3., Copyright 2023 with permission from Elsevier [106]

yields. [27, 75, 116]. However, the concentration of energy from the probe generates an uneven temperature distribution, which can make thermal control difficult in large volume systems and lead to a risk of localized overheating. While the ultrasonic bath offers better thermal stability and reproducibility, its low intensity limits its performance. Based on this, the recommendation is to develop a mixed system that integrates multiple distributed and controlled probes or transducers, allowing scaling volumes to industrial scale, but maintaining efficiency, uniformity, and thermal control in acoustic cavitation.

Laboratory tests require probe systems, which are expensive and more challenging to operate than those used in batch systems but are preferred due to the higher ultrasonic intensity [124]. However, they depend on the probe diameter, viz 25 mm probes have been used for volumes up to 1 L [68]. Therefore, although the ultrasonic bath has lower-intensity implosions than the probe, it is preferred because it generates homogeneous extraction processes for larger sample volumes.

Like other methylxanthine extraction techniques, solvents such as water, ethanol, and methanol are preferred. In the case of ultrasound systems, additives, such as formic acid, control the solvent pH. It has been demonstrated that solvent acidification can enhance the extraction of theobromine. Table 3 shows that acidification with formic acid allows for reaching values between 9.3—12.9 mg g^{-1}, overcoming other studies with non-acidified solvents [73]. Likewise, it is shown that extraction of theobromine is achieved using frequencies around 20 to 40 kHz.

Pulsed electric Field (PEF) and High-Voltage Electric Discharge Extraction (HVED)

Another cavitation extraction technique is the pulsed electric field and the high-electric discharge approach. In these two cases, two electrodes are submerged in a liquid. A high-voltage pulse between the two electrodes generates a moderate electric field (around 20 kV/cm) for the pulse electric field or a high electric field (100 kV cm^{-1}) at high-voltage electric discharge extraction, respectively (Fig. 4). In both cases, the electrical discharge transfers quickly and localized energy into the liquid, producing electric spark bubbles [19]. These bubbles act as cavitation microbubbles that collapse rapidly, producing shock waves [19].

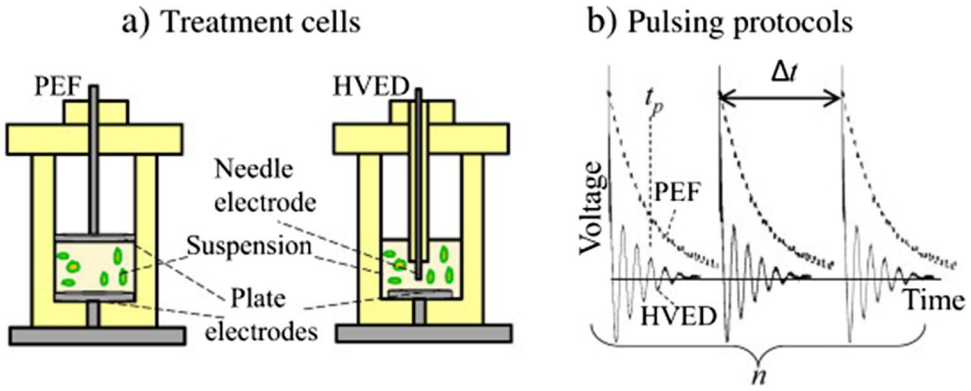

Fig. 4 Pulsed electric fields (PEF) and high voltage electrical discharges (HVED) treatment cells (**a**), pulsing protocols (**b**), and aqueous extraction procedures. Reprinted from *Food Research International, 65 (Part C),* Parniakov, et al. Impact of pulsed electric fields and high voltage electrical discharges on extraction of high-added value compounds from papaya peels, 337–343., Copyright 2014, with permission of Elsevier [91]

Since the pulsed electric field (PEF) technique uses moderate to high electric fields (around 20–80 kV cm^{-1}), i.e., voltage pulses of short duration (from nanoseconds to milliseconds), it is a low-energy consumption extraction approach that offers temporary or permanent membrane permeability [125]. Hence, intracellular compounds from vegetable matrices are released faster, increasing extraction rates and yields. The pulsed electric field approach is highly recommended to extract thermally sensitive compounds or in situations that require extensive cell structure destruction to release the bioactive compounds [71].

For example, Barbosa-Pereira et al. [9] demonstrated that the extraction of polyphenols and methylxanthines from cocoa bean shells (CBS) and coffee silver skin (CS) using pulsed electric field (PEF) showed an increase by around 20%, becoming a new economically viable alternative extraction method. The conditions for phenolic compounds extraction from CBS used by Barbosa-Pereira et al. were 991.28 pulses of 11.99 µs to generate an electrical field strength of 1.74 kV cm^{-1}. Although the authors performed their pulsed electric field extraction in ethanol (39.15%), followed by a solid–liquid extraction time of 118.54 min [9], they were not able to report better efficiencies for the two most prominent methylxanthines, i.e., theobromine or caffeine, when compared with conventional methods.

High-voltage electric discharge extraction (HVED) is characterized by the use of higher electrical fields (40 kV cm^{-1} or more) for microseconds using higher-voltage electrical discharge pulses [78]. Due to its mechanical and electrical effects on the product, HVED produces larger structural damage than PEF with higher cell permeation. It facilitates the extraction process [78], reduces costs, and increases functional properties [11].

Both techniques, HVED and PEF, are less efficient in recovering methylxanthines. It was reported that using HVED (80 Hz for 15 min) in aqueous solutions with 1.5 and 3% CBS extracts methylxanthines less efficiently than phenolic components, which reach up to 84% of theobromine and caffeine. [11]. HVED also influences the hardness of CBS, making them more difficult to grind or refine, which implies a change in fiber properties [10]; this influences the particle size and rheology of the paste during chocolate manufacturing [13]. On the other hand, HVED influences the presence of metals in the CBS residue after treatment, producing a decrease in the content of K, Cd, U, Co, Ni, Fe, Mo, Cr, Mn, and Cu,however, it showed a higher increase in Ca [12].

Advanced Green Solvent Extraction

Currently, there are advanced extractive techniques with pressurized liquids (PLE), supercritical fluids (SFE), subcritical water (SWE), and pressurized hot water (PHWE) that have proven to be highly effective for the recovery of bioactive compounds such as theobromine, surpassing conventional methods in efficiency, selectivity, and sustainability [3, 37, 121]. These techniques were initially developed to be operated in static or batch mode, which implies that the solvent and sample are kept in contact without flow until equilibrium is reached with precise control of the extractive conditions [76]. The evolution towards continuous configurations has broadened its applications and enabled its implementation in larger-scale processes with higher efficiency. This involves a constant flow of fresh solvents through the sample, improving mass transfer and reducing extraction time to prevent thermal degradation of thermosensitive compounds. [76]. However, the theobromine extraction from cocoa using continuous extraction techniques is just being evaluated at laboratory scale. Theobromine extraction from cocoa using continuous extraction techniques has not

been found in previous literature, so further experimental development is required to improve the theobromine recovery efficiency, reduce solvent consumption, and improve its kinetics.

Supercritical CO_2 Extraction (SC-CO_2)

Supercritical fluid extraction (SFE) is gaining popularity as an eco-friendly method for extracting bioactive compounds from diverse botanical sources. Carbon dioxide is the preferred solvent in SFE for extracting volatiles and essential oils due to its low polarity, mild critical conditions, nonflammability, low cost, and ease of removal from the extract [80]. The extraction of bioactive compounds using supercritical fluids (SFE) takes advantage of the properties of CO_2 above its critical point (31.1 °C and 7.38 MPa), being simultaneously gas and liquid, presents high diffusivity, low viscosity, and adjustable density, which facilitates penetration into the plant matrix, allowing mass transfer and efficient extraction. [20, 30, 120]. The preheated supercritical CO_2 flows through the particulate material, transferring heat by convection to the plant solid, which promotes thermal desorption of the metabolite. In this manner, the solvent penetrates the pores of the plant material, solubilizes the metabolite through physicochemical interactions, and facilitates its diffusion into the solvent, driven by concentration gradients [54]. This process can be enhanced by the addition of a polar co-solvent such as ethanol, which improves the affinity of the system towards moderately polar compounds such as theobromine [53, 118].

Supercritical CO_2 extraction is an excellent alternative for obtaining caffeine and fats from ground CBS. Furthermore, it can be used as a sample pretreatment to get higher yields of theobromine [41]. Higher yields of theobromine extraction were achieved at 303 K and 2000 psi, resulting in 17.09 mg g-1, compared to 318 K and 4000 psi, which yielded 15.82 mg g-1, using SC-CO_2 [41].

Although the chemical structures of the xanthines (caffeine, theophylline, and theobromine) are very similar, their dissolution capacities in carbon dioxide in the supercritical state are significantly different. Caffeine has a CO_2 solubility one order of magnitude higher than that of theophylline and two orders of magnitude greater than that of theobromin, applying temperatures around 313—353 K and in a pressure range of 20–35 MPa [62]. Similarly, Saldaña et al. [109] confirmed a higher selectivity for caffeine than theobromine from cocoa beans, which increases recovery time and requires a higher CO_2 solvent amount. Theobromine extraction is enhanced by mixing ethanol with carbon dioxide, reducing pressure, and conserving energy. Varying ethanol content from 5 to 10% with CO_2 increase from 42 to 90% the theobromine content 5.15 and 10.98 g theobromine/kg cocoa beans [109]. In another study, CBS theobromine extraction in an integrated green process comprised of two steps: a supercritical fluid extraction (CO_2 at 20 MPa 40 $°C^{-1}$) and a pressurized liquid extraction (PLE-ethanol at 10 MPa 70 $°C^{-1}$), reported theobromine with a relative area of 46.04%, measured by GC–MS [80].

Subcritical Water Extraction (SWE)

Subcritical water extraction (SWE) is an advanced extraction technique that uses water at elevated temperatures, above its boiling point (100 °C) but below its critical point (374 °C), under pressures sufficient to keep it in the liquid phase throughout the process [23]. This technology can be considered a specific variant of pressurized liquid extraction (PLE), which shares the same thermodynamic fundamentals but allows the use of other organic solvents or binary mixtures. Therefore, subcritical extraction using water (SWE) as an extraction medium is an environmentally friendly solution for extracting various substances without the use of organic solvents or catalysts.

Water under these subcritical conditions exhibits a decrease in its dielectric constant and viscosity, which favors the solubilization of both polar and partially apolar compounds, resulting in faster and more efficient extraction processes with higher yields than those obtained under conventional room temperature conditions. [23].

In subcritical water extraction (SWE), the primary heat transfer mechanism is conduction, whereby thermal energy is initially transferred from the heat source to the aqueous medium and then to the plant matrix. Increasing the water temperature produces several effects, such as improved mass transfer from the solid matrix to the solvent due to increased solubility of the bioactive compounds, especially those of intermediate polarity, as well as a decrease in the surface tension and viscosity of the water, which improves its penetration into the sample pores and facilitates the desorption and diffusion of the compounds. [23].

The SWE of active compounds from cocoa shells demonstrated a steady increase in theobromine concentration from 120 ºC to 170 ºC, along with an increase in antioxidant activity, varying from 15 to 75 min. Furthermore, increased temperatures lead to the extraction of unwanted compounds [63]. The compounds extracted by SWE from CBS include theobromine, theophylline, caffeine, catechin, epicatechin, gallic, and chlorogenic acids, as well as some sugars and their derivatives [63]

Pressurized Hot Water Extraction (PHWE)

In their study, Pagliari et al. [89] calculated the recoveries of pressurized hot water extraction (PHWE) by comparing the amounts of methylxanthine compounds in PHWE extract with those obtained by the ultrasound-assisted extraction

(UAE) technique. Considering the three main compounds of interest (caffeine, theobromine, and antioxidant activity), their chemometric analysis suggested the following parameters as the optimized conditions for PHWE: Temperature 90 °C, Cycles 5, 15% EtOH, and Static Time 6 min. These PHWE parameters offered an improvement in the yield of theobromine, 156.4%, and caffeine, 160.8%, compared to UAE. Pagliari et al. [89] demonstrated that PHWE can provide an exhaustive extraction efficiency that is even more significant than UAE techniques.

Extraction with Deep Eutectic Solvents (DES)

Deep Eutectic Solvents (DES) have higher extraction capacity than conventional solvents [34] by combining at least two compounds that act as a hydrogen bond donor or a hydrogen bond acceptor, such as ammonium compounds and carboxylic acids, respectively [1]. On the one hand, DES presents a more environmentally friendly extraction process for various molecules. On the other hand, one disadvantage is their low vapor pressure, which makes it difficult to separate them from the extracted compounds [34]. Recently, new formulations of deep eutectic solvents (DES) have been developed using primary metabolites and materials of bio-renewable origin, known as natural deep eutectic solvents (NADES), which are based on the use of combinations of sugar alcohols, sugars, amino acids, and organic acids. [127].

Jakovljević et al. [58] demonstrated that DES doesn't offer a better recovery process for theobromine and only slightly improves the recovery of phenolic compounds from CBS. The authors reported that increasing the extraction time from 180 to 360 min in a choline chloride:oxalic acid and H2O 50% solution at room temperature improved the antioxidant activity. Meanwhile, Benítez-Correa et al. [16] demonstrated promising results. By using another DES system (i.e., Choline chloride: Lactic acid 1:2 and 50% H_2O), they obtained higher recovery of theobromine (5.80 mg g^{-1}) and Caffeine (2.08 mg g^{-1}) than when using choline chloride: glycerol and choline chloride: ethylene glycol (both in molar ratio 1:2 and 50% H_2O), and even 70% ethanol.

Combining DESs with ultrasound-probe-assisted extraction (UAE) has proven to be an environmentally friendly alternative to traditional extraction methods (Table 4).

Deep eutectic solvents (DES) have a high viscosity, which limits diffusion and reduces the efficiency of the extraction process, which can be compensated by the use of ultrasound by inducing localized acoustic cavitation and generating turbulent flows, significantly reducing the resistance to mass transfer, facilitating the penetration of the solvent into the plant matrix and accelerating the release of the bioactive compounds. This synergetic effect enables the achievement of higher extractive yields in shorter times, even for poorly soluble or compounds of intermediate polarity, which are traditionally considered insoluble in both water and lipophilic media. Theobromine, being an alkaloid with limited solubility in water, is usually extracted using ethanol as an alternative solvent due to its intermediate polarity, which is capable of solvating functional groups of low molecular weight (–C=O and –CH3) [85, 127]. In this context, the use of NADES represents a promising alternative for the efficient recovery of theobromine from CBS, especially when integrated with intensification technologies such as ultrasound-assisted extraction (UAE).For example, Ruesgas-Ramón et al. [107] applied DES (choline chloride: lactic acid 2:1 and 10% H_2O) in combination with UAE and achieved a higher extraction yield of methylxanthines (i.e., theobromine, caffeine, and chlorogenic acid) than only stirring-assisted extraction (HCR). Likewise, Pavlović et al. [93] demonstrated a higher extraction yield of bioactive compounds from CBS with a combination of microwave-assisted (MAE) and DES extraction.

Other Extraction Technologies

Non-thermal technologies, such as cold atmospheric plasma, have become essential for avoiding quality alterations in color and texture, as well as the consequent loss of nutrients [90]. Cold atmospheric plasma extraction is an economical, versatile, and eco-friendly technique that has proved efficient for removing toxins, decontaminating food, and inactivating enzymes. Still, it is also used to extract bioactive [58].

Plasma is an ionized, quasi-neutral state of gas based on thermal equilibrium, composed of ions, free electrons, atoms, and molecules. Its efficiency depends on the plasma source, electrode design and spacing, pressure, voltage, treatment time, and reactive gas [90]. It has been reported that reducing frequency from 100 to 70 Hz in pure water increases theobromine yield from 4 443 to 5 612 mg kg^{-1} due to the micro rupture of the cell walls produced by cavitation [58].

Ohmic heating extraction produces heat from electricity, providing rapid and uniform heating. In this way, it promotes the heating and electro-permeation of cell membranes, which is essential for extracting biological compounds [110]. Using ohmic heating (2–15 V cm^{-1}), the extraction of phenolic compounds increased by around 40% compared to the conventional technique (0 V cm^{-1}). Additionally, the antioxidant activity ranged from 4 to 20%. It was reported that the maximum extraction of phenolic compounds (23 mg GAE/g CBS) was obtained at 67 °C, 50 min, and 44% ethanol (v/v) [110].

Encapsulation Process and Protection Materials as Encapsulant Agents

The encapsulation process is widely used in the chemical, pharmaceutical, cosmetic, and food industries for protecting nutraceutical compounds that are vulnerable to oxidation

Table 4 Theobromine extraction parameters by cold atmospheric plasma, pressurized liquid, supercritical CO_2, Soxhlet, and deep eutectic solvents (DES)

Extraction method	Raw material	Ratio L/S (mL g^{-1})	Time (min)	Temp (ºC)	Solvent	Specifics conditions	Concentration (mg g^{-1})	Reference
Cold atmospheric plasma extraction	CBS ground	N.I	30	N.I	H_2O	Frequency: 100	4.4 *	[58]
	CBS			N.I		Frequency: 70	5.6 *	
Pressurized-liquid	CBS ground	3	5	75	EtOH absolute	Pressure: 10.35 MPa 1 static cycle Volume cylindrical cell: 100 mL	1.9 **	[88]
			30	90			3.3 **	
			50	90			3.5 **	
	CBS (300–600 µm)	5/1	2	110	EtOH (7.5%)	Five static cycles Pressure flush volume: 69 bar at 150% Purge time: 100 s A total of 4 mm glass beads	20.6 ***	[89]
Supercritical CO_2	CBS ground		30	40	CO_2	Flow: 2 kg h^{-1} Mass: 100 g Pressure: 300 bar	5.9*	[58]
			30	60	CO_2		6.3 *	
	CBS ground			44.85	CO_2	Flow CO_2: 0.176 g min^{-1} Ratio: 3:2 (g EtOH mL^{-1}) 275.8 bar Static and dynamic phase time: 20 min for each one	1.7 ****	[41]
Soxhlet	CBS ground			100	petroleum ether, 5 g 120 mL^{-1}		0.001 *	[58]
With deep eutectic solvents (DES)	CBS ground		60	Room	choline chloride: oxalic acid and H_2O (50%)	Stirring: 1100 rpm	3.6 *	[58]
			360				4.0 *	
	CBS ground	20	140	30	Choline chloride: Lactic acid 1:2 and H_2O (50%)	Magnetically stirred	5.80	[16]
					Choline chloride: Glycerol 1:2 and H2O (50%)		2.59	
					Choline chloride: Ethylene glycol1:2 and H2O (50%)		3.24	
	CBS ground	20	60	50	Choline chloride: Butan 1,4-diole 1:2 and H_2O (50%)	Stirring	3.64	[93]
					Choline chloride: Oxalic acid 1:1 and H_2O (50%)		*3,605*	
					Choline chloride: Urea 1:2 and H_2O (50%)		*3.61*	
	CBS Ground (< 0.5 mm)	5	60	60	Choline chloride: Lactic acid: H_2O 1:2:1.5	Magnetically stirred	4.6	[107]

*HPLC–DAD; **UPLC-MS/MS; ***UPLC-UV; ****UV–Vis

and degradation due to adverse environmental factors [36]. Exploring encapsulation systems that enhance the stability and usefulness of these compounds is crucial for protecting them. Coating materials from various sources and different processing conditions are investigated to obtain micro- and/or nanostructures that protect a bioactive core [36, 61]. These tests range from laboratory level to pilot or industrial scale.

On the other hand, agro-industrial residues are considered secondary and waste materials, which have been extensively studied as sources of functional bioactive molecules, but also represent a sustainable source of polymers such as starch, cellulose, and pectin that can be extracted from husks, seeds, and pulp residues of the processes, and can serve as protective materials in the encapsulation processes of bioactive compounds [4–7, 123]. Likewise, agro-industrial wastes are also inexpensive sources of nutrients, such as sugar cane molasses and sucrose, which have enabled the biological synthesis of biopolymers, yielding xanthan gum and dextran, with the same industrial applications or purposes [103, 123]. Therefore, the opportunity arises to study the physical and rheological properties of these biomaterials, which can be used individually or synergistically, for the protection of bioactives derived from CBS in micro- or nanoencapsulation processes, adopting a circular economy approach.

Microencapsulation of Cocoa by-Product Bioactive

The spray-drying microencapsulation technique is used for stabilizing CBS extracts. This technology is low-cost and straightforward, facilitating large-scale adoption in the industry [104]. Despite being a widely used and effective technique to stabilize bioactive compounds, we identify methodological limitations: most research prioritizes the evaluation of total phenols and antioxidant capacity, while the specific quantification of alkaloids, such as theobromine, is scarce or absent, which limits our understanding of the encapsulation behavior of these key compounds. Another aspect is the use of materials studied for encapsulating bioactives from other botanical sources, where encapsulation processes with maltodextrin (MD) stand out, becoming the most commonly used material for encapsulating bioactives at the laboratory or pilot level. Nevertheless, MD could be replaced or combined with chitosan (CH), gum Arabic (GA), carrageenan (CR), gelatin (GL), and goat milk whey (GMW), as shown in Table 5. After encapsulation, spectrophotometric techniques enable the evaluation of the protective material's efficiency. For example, extract contents are evaluated according to their total phenolic compounds (CFT, mg GAE/g dw), total flavonoid content (CTF, mg RE/g dw or mg CE/g), and antioxidant capacity. The latter is measured based on the 1,1-diphenyl-2-picrylhydrazyl (DPPH) method, ferric reducing antioxidant power (FRAP) assay, or ABTS (2,2-azino-bis-(3-ethylbenzothiazoline-6-sulphonic acid)) radical cation scavenging activity assay.

Maltodextrin

Maltodextrin (MD), measured in dextrose equivalent (DE), is a highly demanded additive in the food industry for encapsulating cocoa products. [47] It protects against oxidation, provides a smoother mixture for pulverization, has a mild flavor, and is water-soluble. Maltodextrin (MD) is the most commonly used excipient due to its availability and properties, which are suitable for spraying, and has been used as an encapsulation enhancer with different dextrose equivalents (DE) for bioactive protection. However, its excessive use may reduce the final bioactivity of the powder due to the decrease in the antioxidant capacity as the coating ratios increase to improve the process yield. Some experiences are listed below. For instance, MD (DE 17.0–19.9) encapsulated CBS extracted dissolved in water (10%, w/v) at three different concentrations (core/coating ratio 1:5, 1:10, and 1:15 W:W) was produced using the spray-drying (inlet temperature: 150 °C; flow rate: 87 6 ml/min). A microencapsulated powder with CFT (22 mg kg^{-1}), a mass yield of 78.1%, and antioxidant activity of 64% (DPPH) with a core: coating agent ratio of 1:5 of 1 g of lyophilized CBS extract [45]. Likewise, the stability of CBS extracts obtained with MD (DE16) and whey protein isolated (WPI) generated higher TP and TF (37.68 mg GAE/g and 7.66 mg CE/g, respectively) using subcritical water extraction and spray drying. However, theobromine extraction was higher using WPI than MD (7.3 vs. 6.0 mg/g). On the other hand, methylxanthines are better preserved using a coating with 50% WPI and CBS powder recovery with 50% MD formulation (73.52% vs 58.61%) [64]. Furthermore, MD with a higher dextrose equivalent (DE20) was compared with goat milk whey (GMW) as an encapsulating agent for cocoa powder bioactive (1:1 ratio in 200 ml of water). GMW recovered more bioactive during spray-drying than MD (33.11% vs. 24.03%) and got higher phenolic compound content than MD. Nevertheless, there is no difference in antioxidants [114].

Encapsulation cocoa pods (CPH) extract in ethanol with different MD concentrations has a powder drying yield of 32% (20% MD and 80% ethanolic extract) that reaches up to 70% (60% MD and 40% extract) with MD increase by spray drying (inlet temperature: 150 ºC, feed flow: 10 ml/minute). On the other hand, antioxidant activity is negatively affected by increasing MD, varying the anti-oxidant-containing compounds (IC 50) from 75.89 to 114.89 µg/mL [48]. In other studies, crude *cupuassu* (*Theobroma grandiflorum*) seed extract was dissolved in 50 mL of 50% (w/v) ethanolic solution with 100, 150, or 200 g L^{-1} maltodextrin (MD), to obtain extracts containing 5.0, 7.5, or 10.0% (w/v) MD. Higher retention of around CFT (80%) and CTF

Table 5 Encapsulation process and conditions of theobromine extracts (cocoa bean shells, CBS; cocoa shell powder (CSP); cocoa pod husk (CPH); DV: mean diameter over volume; V/S: volume/surface mean. GAM: gum Arabic microcapsule; MDM, maltodextrin microcapsule; GMM, gum Arabic + maltodextrin microcapsule. IN: Inlet air temperature, OUT: Outlet air temperature, F: feed pump flow rate, DAF: dry airflow)

Raw material	Extraction process	Encapsulation compounds	Atomization/pulverization	Dry conditions	Capsules		References
					Size	Morphology	
Seeds cocoa ground defatted (hexane/24 h)	Ultrasonic bath (H_2O/EtOH 1:1) or (acetone/H_2O 70:30) vacuum concentrated and lyophilized	Pectin + WPI	Aspersion nano-dryer with 4 µm grid	IN: 120 °C OU: 65 °C F: 3 mL h^{-1} DAF: 100 L min^{-1}	SEM: 530 nm	Spherical	[2]
Seeds copoazu (Theobroma grandiflorum) roasted, pressed, dehydrated, pulverized	Percolation extraction [ethanol/H_2O 70:30 (v/v)] and vacuum concentration	MD 5.0% (w/v)	Mini spray dryer with 0.5 mm nozzle diameter	IN: 170 °C, F: 5.0 mL min^{-1} DAF: 32.5 m^3 h^{-1}	SEM: 274.7 nm	Spherical	[31]
Powder residue of Cocoa bean pressing	Percolation extraction [ethanol/H_2O 70:30 (v/v)] and vacuum concentration	CH 0.5% (v/w) + 5% MD	Mini spray dryer	IN: 170 C MD del 5% F: 2.5 mL min^{-1}.DAF: 30 mm Hg	SEM: 0.19—5.93 µm	Spherical, smooth, no clusters or crackers	[39]
Cocoa-based products	N.D	MD/goat milk whey (GMW)	B-290 mini spray dryer with 1.0 mm standard diameter nozzle	IN: 160 °C F:30% Evaporation capacity: 1.0 L h^{-1}	CM size 21.92 and CW size 21.12 µm		[114]
CBS < 250 µm	Ultrasonic bath	MD (DE: 17.0–19.9)	Mini Spray Dryer with a co-current two-fluid nozzle	IN: 150 °C F: 6 ml min^{-1} Aspiration rate: 28 $m^{3\ h-1}$	volume distribution D 30.6 µm	N.R	[45]
Cocoa husk (100 mesh)	Liquid–solid phase extraction	20% MD suspension (stirred 5 min at 13 000 rpm)	spray-dryer	IN: 150 ºC F: 10 ml min^{-1}	N.R	N.R	[48]
CSP (50-mesh)	Liquid–solid phase extraction	GA + MD	spray-dryer	IN: 155 °C OU: 90 °C F: 10 °C, DAF: 1.54 m^3 min^{-1}	GAM: 8 y 80 µm DV: 31 µm V/S: (3,2) 15.50 MDM: 6 y 110 DV: 31.90 V/S: 14.60 GMM (GA + MD): 11 y 80 µm DV: 34.30 V/S: 18.50	Smooth surfaces, spherical, no dents or pleats	[57]
CBS	SWE	MD + WP	Anhydro spray dryer (Anhydro AS, Denmark)	IN: 120 °C OU: 75–80 °C Atomizer speed: 20,000 to 21,000 rpm	N.R	N.R	[64]

Table 5 (continued)

Raw material	Extraction process	Encapsulation compounds	Atomization/pulverization	Dry conditions	Capsules		References
					Size	Morphology	
CPH	MAE vacuum concentrated	(100): MD (80:20): MD:GA (80:10:10): MD:GA:CH; MD:GA:CR; MD:GA:GL	Lyophilized	Temperature: −40 °C Pressure: 0.001 mbar for 2 days	N.R	Irregular shapes and various sizes	[87]
CPH (size ≤ 1.0 mm)	MAE vacuum concentrated	(100): MD (90:10):MD:GA (80:20): MD:GA (80:10:10): MD:GA:CH	Freeze dryer	Temperature: −40 °C Pressure: 0.001 mbar for 2 days	N.R	surface structure in terms of folds, shrinkage, or dents	[86]

MAE microwave-assisted extraction; whey protein isolated, *WPI*, *CH* chitosan, *MD* maltodextrin, *GA* gum Arabic

(82%) was achieved with 5% w/v MD concentration (inlet temperature: 170 °C; feed flow rate: 7.5 mL min^{-1}), obtaining microencapsulation powder with CFT (33 mg GAE/g) and CTF (12 mg CE/g), and drying yield of 12.6%. Drying yield could be improved to 19% using MD at 10% w/v (inlet temperature: 160 °C; feed flow rate: 5.0 mL min^{-1}) to the detriment of CFT and CTF retention up to 67% [31]. The HPLC–DAD chemical profile reported for the encapsulation with higher dryer yield: gallic acid (2.2 mg 100 g^{-1}), glycosylated quercetin (39.8 mg 100 g^{-1}), protocatechuic acid (15.5 mg 100 g^{-1}), p-coumaric acid (2.2 eg 100 g^{-1}), epicatechin (39.8 mg 100 g^{-1}) and epigallocatechin gallate (8.8 mg 100 g^{-1}) [31]. Theobromine was not quantified.

Synergistic Effect of MD with Other Biomaterials

Maltodextrin (MD), when combined with other biopolymers such as gum arabic (GA) and chitosan (CH), generates highly synergistic multicomponent coating systems, significantly improving the encapsulation efficiency and stability of bioactive compounds, evidencing high retention of bioactive compounds and superior antioxidant activity, and represents an advanced and effective strategy to obtain functional microencapsulates with applications in cocoa-derived nutraceutical systems. Combinations of mucilages, hydrocolloids, or starches have become popular due to higher bioactive encapsulation efficiencies, generating less porous matrices and delaying the release of these compounds [42]. Specifically, whey protein isolate (WPI), goat milk whey (GMW), chitosan (CH), gum Arabic (GA), pectin (P), starch (H), and maltodextrin (MD) have been applied as protective co-materials for cocoa extracts and derivatives. [112]. The emergence of emerging materials such as WPI, GMW, CH, and their mixtures has shown improvements in the recovery of bioactive compounds, but their standardization and technological compatibility still require further validation for the stability of cocoa-derived alkaloids. In the literature, it is reported that microcapsules with modified starch (HC) have a higher number of semispherical morphologies in comparison to microcapsules with maltodextrin (MD) with a size varying from 5 to 15 µm [112].

Cold-pressed cocoa bean powder extracted was encapsulated by atomization mixing 5.0% (v/v) cocoa extract, 0.5% CH (v/p), and 5.0% MD (v/p) in a spray drying process (inlet temperature: 170 ºC, extract flow rate: 2.5 mL min^{-1}; aspiration rate: 80% (32 m^3 h^{-1}); airflow: 30 mm Hg). In addition, antioxidant activity from extracted was reduced after encapsulation from 1905 to 623.76 µM Trolox g^{-1} [38]. Likewise, pressed cocoa bean extract microencapsulation was optimized using CH and MD as protective co-materials. 5% MD (DE 16.5–19.5) and 0.5% CH (v/w) were mixed (inlet temperature: 170 ºC,extract flowrate: 2.5 mL min^{-1}). HPLC analysis identified epicatechin as

the major component of both extracts (24.0 mg g^{-1}). The microcapsules presented a TPC of 80 mg GAE/g, gallic acid (1.35 mg g^{-1}), protocatechuic acid (0.93), catechin (4.30), vanillic acid (8.33), epigallocatechin and gallate (1.85) [39]. In addition, MD, GA, and a mixture were used as protection material for the cocoa husk extract (40% w/v in a 1:2 w/w ratio) (inlet temperature: 155 °C,flow rate: 1.54 m^3 min^{-1}). MD microcapsule presented higher TPC (169.09 mg GAE 100 g^{-1}) and TFC protection (114.69 mg QE 100 g^{-1}). However, the mixture produced the highest DPPH values (1063 mM Trolox 100 g^{-1}) compared to each microcapsule of a single material, taking advantage of synergistic protection effects [57].

Lyophilization, also known as freeze-drying, is another thermosensitive bioactive encapsulation method based on sublimation dehydration. Despite being used in designing high-value-added products with bioactive compounds of higher biological activity, this technique is not economical due to its lengthy process (24–48 h) [102]. On the other hand, it is a simple technique (with few steps) compared to microencapsulation methods such as coacervation, solvent extraction, and supercritical fluid precipitation, among others [99, 102]. Furthermore, there is little evidence of research that directly compares technologies, such as spray-drying and freeze-drying, nor does it discuss aspects of industrial scalability or stability during storage, focusing primarily on the quantification of total bioactives and their antioxidant capacity. For instance, microencapsulation by freeze-drying (−40 °C and 0.001 mbar) of cocoa shell extract (CPH) using MD with GA, CH, carrageenan, or gelatin as coating materials was investigated. For this purpose, the materials were previously hydrated (1:1 v/w) and mixed with CPH extract in a 1:1 (w/w) ratio. Both coating material MD and MD: GA (8:2 w/w) retained, with non-significant differences, the highest levels of total phenols (~ 15.51 mg GAE/g), flavonoids (~ 24.96 mg CE/g), saponins (~ 307. 13 mg EE/g); and alkaloid (463.47 and 494.55 mg GAE/g) [87]. Similarly, freeze-drying on microencapsulation of cocoa shell extract (CPH) was mixed with MD and GA or CH previously dissolved in water (1:1 v/w) at a ratio of 1:1 (w/w). MD and GA (9: 1 w/w) retain the highest levels of TPC (14.91 mg GAE), TFC (22.69 mg CE), TSC (113.21 mg EE), and using MD 100% resulted in maximum amounts of TAC (646.96 mg AE/g ds) and ARSC (36 mg TE/g ds) [86].

Nanoencapsulation of Cocoa by-Product Bio-Actives

Nanoencapsulation represents an emerging technological strategy for protecting and transporting bioactive compounds derived from cocoa by-products, highlighting its applicability in functional and nutraceutical matrices. Nanoencapsulation coats bioactive compounds in liquid, solid, or gaseous form inside an inert material to protect, stabilize, and control their release through specific active areas (Table 5). It requires a particle size of less than 1000 nm to be classified as nanoparticles, which, due to their size, vary significantly in their physicochemical properties compared to microparticulate or bulk materials. [72, 92]. Nanoscale encapsulation of antioxidants, antimicrobials, vitamins, probiotics, prebiotics, minerals, enzymes, and other compounds has enabled the development of flavorings, food ingredients, and nutraceuticals. For this reason, it has been applied as protective materials, such as carbohydrate-, protein-, or lipid-based materials, including chitosan nanoparticles, chitosan peptides, and β-lactoglobulin or biopolymer emulsion mixtures [92]. On the other hand, considering theobromine, a compound partially limited by its polarity and low solubility in non-aqueous media, other types of nano transporters, complemented with nano-spray drying, could be evaluated. For example, nanoemulsions, solid nano-lipids, and self-assembled natural polymers, which have not been previously reported for cocoa extracts, could be considered.

y polímeros naturales autoensamblados, que no se reporta para extractos de cacao.

The use of biocompatible and functional materials, such as pectin and whey protein isolate (WPI), offers structural and functional synergies in terms of colloidal stability and antioxidant capacity within the system. Both materials have been used as bioactive protection materials for cocoa cotyledon extracts on the nanoscale. The nanoparticle solution comprised 2.5% P, 0.25% WPI, 0.004% Tween 80, and 0.05% freeze-dried cocoa extract. Nanoparticles loaded with polyphenolic extracts obtained by spray-drying (inlet temperature: 120 °C; feed rate: 3 mL h^{-1}; drying gas flow rate: 100 L min^{-1}) were characterized by a 530 nm particle size, a CFT of 91.53 mg GAE/g, and antioxidant activity (EC50) of 50.21% [2]. The cocoa industry can effectively utilize pectin in nanoencapsulation processes, as the CPH fruit shell, the primary waste product, contains pectin with a low degree of methoxylation (LM), allowing the encapsulation of compounds sensitive to high temperatures or extreme pH levels [6, 33, 122].

Other natural extracts have also been nanoencapsulated by spray drying. For example, tests on Opuntia atropes extracts with different encapsulating agents (maltodextrin, soy protein isolate, calcium caseinate, alone and in combination with MD) show that MD produces spherical, nanometric, and well-defined capsules, with particle sizes ranging from 110 to 405 nm [117]. Therefore, although the approach is promising, interactions between the wall material and the encapsulated compounds must be evaluated, as well as on the critical conditions of spray drying at the nanoscale, as the efficiency is usually lower than in microencapsulated systems due to the higher risk of thermal degradation and coalescence or melting of droplets during encapsulation of

cocoa-specific compounds such as theobromine, polyphenols or catechins.

Conclusions and Future Prospects

In conclusion, using emerging agricultural residues from the cocoa industry, such as cocoa bean hulls (CBS), presents an interesting opportunity for sustainable utilization in the nutraceutical industry. These agricultural residues, rich in bioactive compounds such as polyphenols and methylxanthines, have shown significant potential to promote health benefits, ranging from antioxidant and anti-inflammatory effects to their possible role in preventing kidney stone formation due to the presence of theobromine.

Although polyphenol recovery has been the primary focus in the literature, there is a growing need to develop and optimize methods for extracting and stabilizing other predominant compounds in CBS, such as theobromine. These compounds could be incorporated into functional foods and pharmaceuticals, providing new non-surgical treatments for diseases such as kidney stones.

Extraction technologies, especially those considered environmentally friendly or "green processes" due to their short extraction periods and non-toxic solvents, offer promising avenues for efficiently recovering these bioactive compounds. Although extraction technologies (such as SWE, SFE, PLE, and EAU) and encapsulation methods, including lyophilization and nano spray drying, are promising at the laboratory level, their industrial-scale up faces significant technical and economic challenges. Besides the initial high investment cost, such as supercritical fluid extraction (SFE) or nanometric encapsulation, operational complexity requires trained technical personnel. In addition, heterogeneous cocoa by-products, which depend on agronomic factors that complicate the reproducibility of the processes, are evidenced in the variation of theobromine concentration among different studies. Process intensification technologies will depend on improvements in extraction efficiency, reduction of energy costs, and validation of the functionality of encapsulated compounds under real application conditions. For example, by optimizing hybrid or combined processes (e.g., ultrasound-DES), identifying organic solvents that are more compatible with extractive processes (e.g., less viscous NADES), and testing with continuous equipment that is adaptable to industrial volumes.

On the other hand, the encapsulation of CBS bioactives, which relies on the use of maltodextrin (MD) as a wall material, lacks specific characterization of methylxanthines, and a limited evaluation of the release and functionality of the encapsulated compounds hinders progress towards specific nutraceutical or pharmacological applications. The use of MD produces an inverse relationship between the proportion used in encapsulation and the biological activity of the microencapsulated powder. At the technological level, spray-drying encapsulation processes can induce partial degradation of thermostable compounds in CBS extracts. In contrast, techniques such as freeze-drying offer better retention of bioactives, but are still economically limited in the industry due to high energy consumption and lengthy processing times. For this reason, it is essential to utilize MD in conjunction with other emerging materials to enhance encapsulation efficiency and oxidative stability. Still, it requires technological validation in the encapsulation of theobromine-rich CBS extracts, accompanied by higher-resolution structural characterization of theobromine using techniques such as LC–MS. In order to facilitate its implementation at pilot-industrial scale, a comprehensive understanding of the biopharmaceutical behavior of the encapsulated systems is required.

Overcoming these aspects, microencapsulation is the most promising strategy for stabilizing and valorizing bioactive compounds, such as theobromine. It is concluded that the development of functional microencapsulations of theobromine, a potential nutraceutical, will require a more integrative approach, combining experimental design, advanced characterization, release, and bioavailability studies in simulated or real physiological conditions to validate the functional or therapeutic effects of theobromine extracted or encapsulated from cocoa by-products.

Microwave-assisted extraction, cavitation extraction, and advanced green solvent extraction have proven to be efficient in the recovery of bioactive compounds present in CBS, mainly due to the extensive structural damage of the cell walls, improving theobromine extraction performance than solvent extraction and traditional techniques, but still, the scaling up of these technologies needs to be explored to contribute to zero waste policies (i.e., maximizing the value of cocoa industry waste).

In addition, micro- and nanoencapsulation techniques have proven efficient in conserving bioactive present in cocoa residues. However, they have focused on optimizing the stabilization of polyphenols and their antioxidant activity, with maltodextrin as the main protection material. The goal is to improve encapsulation efficiency, develop less porous matrices, and delay the release of compounds using new or mixed compounds such as mucilage, hydrocolloids, starches, or protein isolates, which can also be recovered from other wastes or sustainable resources.

Despite considerable progress in extraction and stabilization technologies for harnessing CBS, from our perspective, there is a gap in the widespread application and adoption of these methods at the industrial level. Furthermore, we believe that further optimization of extraction processes, standardization of protocols, and a deeper understanding of bioactive stabilization and incorporation into consumer

products are necessary to integrate into the industry successfully. By bridging the gap between scientific research and industrial application, we can ensure that these technologies operate at their optimal potential in the recovery and preservation of bioactive compounds, thereby contributing to a more sustainable circular agricultural economy.

Acknowledgements The authors gratefully acknowledge the financial support of the National Program for Scientific Research and Advanced Studies (PROCIENCIA) of the National Council for Science, Technology and Technological Innovation (CONCYTEC) through Project Contract No. PE501086489-2024-PROCIENCIA. The Vice-Rectorate provided additional funding for Research of the Pontifical Catholic University of Peru (PUCP) through the CAP 2024 – PI1115 project. Erick Alvarez-Yanamango also acknowledges the support of the Doctoral Scholarship in Engineering awarded by PUCP.

Author Contribution E.A.Y.: Funding acquisition, Investigation, Conceptualization, Methodology, Project administration, Resources, Writing – original draft, Visualization. D.O.: Investigation, Methodology, Formal analysis, Writing – review & editing, Data curation, Validation. A.I.: Formal analysis, Writing – review & editing, Supervision, Validation.

Funding Open access funding provided by Pontificia Universidad Catolica del Peru. The authors acknowledge the financial support of the National Program for Scientific Research and Advanced Studies (PROCIENCIA) of the National Council of Science, Technology and Technological Innovation (CONCYTEC) through the project with contract PE501086489-2024-PROCIENCIA and the Doctoral Scholarship in Engineering from the Pontifical Catholic University of Peru (PUCP).

Data Availability No datasets were generated or analysed during the current study.

Declarations

Ethical Approval Not applicable.

Clinical Trial Number Not applicable.

Competing interests The authors declare no competing interests.

References

1. Abbott AP, Boothby D, Capper G, Davies DL, Rasheed RK (2004) Deep eutectic solvents formed between choline chloride and carboxylic acids: versatile alternatives to ionic liquids. J Am Chem Soc 126(29):9142–9147. https://doi.org/10.1021/ja048266j
2. Aguilar-Méndez MÁ, San Martín Martínez E, Yáñez-Fernández J, Navarro-Cerón E (2020) In *Avances de investigación en Nanociencias, Micro y Nanotecnologías* - Nanoencapsulación de compuestos bioactivos con actividad antioxidante de Justicia spicigera (Muicle) y Theobroma cacao L. (Cocoa). OmniaScience. https://doi.org/10.3926/oms.404.2
3. Alvarez-Rivera G, Bueno M, Ballesteros-Vivas D, Mendiola JA, Ibañez E (2019) Pressurized liquid extraction. In Liquid-Phase Extraction. Elsevier, pp 375–398. https://doi.org/10.1016/B978-0-12-816911-7.00013-X
4. Alvarez-Yanamango E, Huanqui GC, Huayta F (2020) Recovery and characterization of Lucuma seed starch (Pouteria lucuma) with potential industrial application. Proceedings of the LACCEI International Multi-Conference for Engineering, Education and Technology. https://doi.org/10.18687/LACCEI2020.1.1.587
5. Alvarez-Yanamango E, Vietti F, Huayta F (2018) Use of waste from the processing of Sanky pulp (Corryocactus brevistylus) to obtain a food additive. Proceedings of the LACCEI International Multi-Conference for Engineering, Education and Technology, 2018-July. https://doi.org/10.18687/LACCEI2018.1.1.412
6. Aparicio Huablocho JA, Neira Montoya EF, Ramos Matias PM (2024) Extracción de pectina a partir de la cáscara de cacao y su caracterización mediante análisis de FT-IR. TECNIA 34(1):42–50. https://doi.org/10.21754/tecnia.v34i1.2113
7. Bakantiche DI, Momade Z (2022) Production and characterisation of pectin from cocoa bean shells. Int J Adv Res 5(1):161–173. https://doi.org/10.37284/ijar.5.1.979
8. Barbosa-Pereira L, Belviso S, Ferrocino I, Rojo-Poveda O, Zeppa G (2021) Characterization and classification of cocoa bean shells from different regions of Venezuela using HPLC-PDA-MS/MS and spectrophotometric techniques coupled to chemometric analysis. Foods. https://doi.org/10.3390/foods10081791
9. Barbosa-Pereira L, Guglielmetti A, Zeppa G (2018) Pulsed electric field assisted extraction of bioactive compounds from cocoa bean shell and coffee silverskin. Food Bioproc Tech 11(4):818–835. https://doi.org/10.1007/s11947-017-2045-6
10. Barišić V, Flanjak I, Kopjar M, Benšic M, Jozinovic A, Babic J, Subaric D, Milicevic B, Doko K, Jašic M, Ackar Đ (2020) Does high voltage electrical discharge treatment induce changes in tannin and fiber properties of cocoa shell? Foods 9(6). https://doi.org/10.3390/foods9060810
11. Barišić V, Flanjak I, Križić I, Jozinović A, Šubarić D, Babić J, Miličević B, Ačkar Đ (2020) Impact of high-voltage electric discharge treatment on cocoa shell phenolic components and methylxanthines. J Food Process Eng. https://doi.org/10.1111/jfpe.13057
12. Barišić V, Kerovec D, Flanjak I, Jozinović A, Babić J, Lončarić Z, Šubarić D, Miličević B, Ačkar Đ (2022) Effect of high-voltage electrical discharge treatment on multi-element content in cocoa shell and chocolates with cocoa shell. LWT. https://doi.org/10.1016/j.lwt.2021.112944
13. Barišić V, Petrović J, Lončarević I, Flanjak I, Šubarić D, Babić J, Miličević B, Doko K, Blažić M, Ačkar Đ (2021) Physical properties of chocolates enriched with untreated cocoa bean shells and cocoa bean shells treated with high-voltage electrical discharge. Sustainability 13(5):1–14. https://doi.org/10.3390/su13052620
14. Bautista O (2020) Optimización de extracción de teobromina asistida por ultrasonido a partir de residuos de la industria de cocoa (Theobroma cacao). Bachelor's thesis, Universidad Nacional del Centro del Perú, Huacayo
15. Belwal T, Cravotto C, Ramola S, Thakur M, Chemat F, Cravotto G (2022a) Bioactive compounds from cocoa husk: extraction, analysis and applications in food production chain. Foods. https://doi.org/10.3390/foods11060798

16. Benítez-Correa E, Bastías-Montes JM, Acuña-Nelson S, Muñoz-Fariña O (2023) Effect of choline chloride-based deep eutectic solvents on polyphenols extraction from cocoa (Theobroma cacao L.) bean shells and antioxidant activity of extracts. Curr Res Food Sci 7:100614. https://doi.org/10.1016/j.crfs.2023.100614
17. Benítez-Correa E, Bastías-Montes JM, Nelson SA, Iznaga TB, Wong MP, Muñoz-Fariña O (2024) Improving the composition and bioactivity of cocoa (*Theobroma cacao* L.) bean shell extract by choline chloride-lactic acid natural deep eutectic solvent extraction assisted by pulsed electric field pre-treatment. Plant Foods Hum Nutr 79:351–358. https://doi.org/10.1007/s11130-024-01163-0
18. Bogue J, Collins O, Troy AJ (2017) In: Debasis D, Sreejayan N (eds) Developing New Functional Food and Nutraceutical Products Chapter 2: Market analysis and concept development of functional foods 29–45. Elsevier. https://doi.org/10.1016/B978-0-12-802780-6.00002-X
19. Boussetta N, Lebovka N, Vorobiev E, Adenier H, Bedel-Cloutour C, Lanoisellé JL (2009) Electrically assisted extraction of soluble matter from chardonnay grape skins for polyphenol recovery. J Agric Food Chem 57(4):1491–1497. https://doi.org/10.1021/jf802579x
20. Budisa N, Schulze-Makuch D (2014) Supercritical carbon dioxide and its potential as a life-sustaining solvent in a planetary environment. Life (Basel) 4(3):331–340. https://doi.org/10.3390/life4030331
21. Cacace JE, Mazza G (2003) Mass transfer process during extraction of phenolic compounds from milled berries. J Food Eng 59(4):379–389. https://doi.org/10.1016/S0260-8774(02)00497-1
22. Carrez MC (1908) Le ferrocyanure de potassium et l'acétate de zinc comme agents de défécation des urines. Ann Chim Anal 13:97–101
23. Castro-Puyana M, Herrero M, Mendiola JA, Ibáñez E (2013) Subcritical water extraction of bioactive components from algae. In Functional Ingredients from Algae for Foods and Nutraceuticals. Elsevier Ltd, pp 534–560. https://doi.org/10.1533/9780857098689.3.534
24. Carpentieri S, Soltanipour F, Ferrari G, Pataro G, Donsì F (2021) Emerging green techniques for the extraction of antioxidants from agri-food by-products as promising ingredients for the food industry. Antioxidants 10(9):1417. https://doi.org/10.3390/antiox10091417
25. Cecilia M, Soledad R (2023) Extracción asistida por microondas de compuestos fenólicos de los subproductos del beneficio del cocoa (Theobroma cacao L.). Universidad Nacional de Colombia
26. Chattaraj KG, Paul S (2019) Inclusion of theobromine modifies uric acid aggregation with possible changes in melamine-uric acid clusters responsible for kidney stones. J Phys Chem B 123(49):10483–10504. https://doi.org/10.1021/acs.jpcb.9b08487
27. Chemat F, Rombaut N, Sicaire AG, Meullemiestre A, Fabiano-Tixier AS, Abert-Vian M (2017) Ultrasound assisted extraction of food and natural products. Mechanisms, techniques, combinations, protocols and applications. A review. In Ultrasonics Sonochemistry, Elsevier B.V. Vol. 34, pp 540–560. https://doi.org/10.1016/j.ultsonch.2016.06.035
28. Ciriminna R, Scurria A, Pagliaro M (2023) Natural product extraction via hydrodynamic cavitation. Sustain Chem Pharm 33:101083. https://doi.org/10.1016/j.scp.2023.101083
29. Costa-Bauzá A, Calvó P, Hernández Y, Grases F (2023) Efficacy of theobromine and its metabolites in reducing the risk of uric acid lithiasis. Int J Mol Sci. https://doi.org/10.3390/ijms241310879
30. Cvejić, J. H., Krstonošić, M. A., Bursác, M., & Miljić, U. (2017). Polyphenols. In Nutraceutical and functional food components: effects of innovative processing techniques, Elsevier Inc, pp 203–258. https://doi.org/10.1016/B978-0-12-805257-0.00007-7
31. da Costa RS, Teixeira CB, Gabbay Alves TV, Ribeiro-Costa RM, Casazza AA, Aliakbarian B, Converti A, Silva Júnior JOC, Perego P (2019) Optimization of spray drying conditions to microencapsulate cupuassu (*Theobroma grandiflorum*) seed by-product extract. Nat Prod Res 33(18):2600–2608. https://doi.org/10.1080/14786419.2018.1462178
32. Darasia, Mahendradatta M, Hasizah A, Rahmaniar (2023) Comparison of soxhletation and Microwave Assisted Extraction method for extracting polyphenols in cocoa pod husks (Theobroma cacao L.). IOP Conf Ser: Earth Environ Sci 1200(1). https://doi.org/10.1088/1755-1315/1200/1/012038
33. De Laet E, Bernaerts T, Mikhalski M, Van Loey AM (2024) Kinetic study of a conventional and ultrasound-assisted extraction of pectin from different plant-based side streams: impact on pectin extraction yield, purity and molecular pectin structure. LWT. https://doi.org/10.1016/j.lwt.2024.116522
34. Della Posta S, Gallo V, Gentili A, Fanali C (2022) Strategies for the recovery of bioactive molecules from deep eutectic solvents extracts. TrAC Trends Anal Chem 157:116798. https://doi.org/10.1016/j.trac.2022.116798
35. Djali M, Santasa K, Indiarto R, Subroto E, Fetriyuna F, Lembong E (2023) Proximate composition and bioactive compounds of cocoa bean shells as a by-product from cocoa industries in Indonesia. Foods. https://doi.org/10.3390/foods12173316
36. Fabela-Morón MF, Pérez-Ruíz RV, Ruíz-Hernández R, Arce-Vázquez MB, Aguilar-Toalá JE, Jiménez -Guzmán J, García-Garibay JM (2022) Encapsulation of bioactive compounds of food interest: applications, current advances, challenges, and opportunities. Agro Productividad. https://doi.org/10.32854/agrop.v15i10.2407
37. Fraguela-Meissimilly H, Bastías-Monte JM, Vergara C, Ortiz-Viedma J, Lemus-Mondaca R, Flores M, Toledo-Merma P, Alcázar-Alay S, Gallón-Bedoya M (2023) New trends in supercritical fluid technology and pressurized liquids for the extraction and recovery of bioactive compounds from agro-industrial and marine food waste. In Molecules 28(I11). MDPI. https://doi.org/10.3390/molecules28114421
38. Gabbay Alves TV, Silva da Costa R, Aguiar Gomes AT, Ferreira da Costa CE, Perego P, Carréra Silva Júnior JO, Converti A, Ribeiro Costa RM (2018) Quality control of Amazonian cocoa (*Theobroma cacao* L.) by-products and microencapsulated extract by thermal analysis. J Therm Anal Calorim 134(2):993–1000. https://doi.org/10.1007/s10973-018-7300-1
39. Gabbay Alves TV, Silva da Costa R, Aliakbarian B, Casazza AA, Perego P, Carréra Silva Júnior JO, Ribeiro Costa RM, Converti A (2017) Microencapsulation of Theobroma cacao L. waste extract: optimization using response surface methodology. J Microencapsulation 34(2):111–120. https://doi.org/10.1080/02652048.2017.1296499
40. Geraets L, Moonen HJJ, Wouters EFM, Bast A, Hageman GJ (2006) Caffeine metabolites are inhibitors of the nuclear enzyme poly(ADP-ribose)polymerase-1 at physiological concentrations. Biocheml Pharmacol 72(7):902–910. https://doi.org/10.1016/j.bcp.2006.06.023
41. González-Alejo FA, Barajas-Fernández J, García-Alamilla P (2019) Extracción de compuestos solubles de la cascarilla de cocoa con CO2 supercrítico Caso de metilxantinas y grasa. CienciaUAT 13(2):128. https://doi.org/10.29059/cienciauat.v13i2.1073
42. González A, Navarro A, López J (2023) Sistemas de encapsulamiento a base de compuestos bioactivos de yerba mate y cocoa para la vehiculizarían y protección de multinutrientes.

Invest Joven 10 (esp):186. Resúmenes - EBec UNLP 2022, La Plata. https://sedici.unlp.edu.ar/handle/10915/145705
43. González-Nuñez LN, Cañizares-Macías MP (2011) Focused microwaves-assisted extraction of theobromine and caffeine from cocoa. Food Chem 129(4):1819–1824. https://doi.org/10.1016/j.foodchem.2011.05.118
44. Goya L, Kongor JE, de Pascual-Teresa S (2022) From cocoa to chocolate: effect of processing on flavanols and methylxanthines and their mechanisms of action. Int J Mol Sci 23(22):14365. https://doi.org/10.3390/ijms232214365
45. Grassia M, Messia MC, Marconi E, Şakiyan Demirkol Ö, Erdoğdu F, Sarghini F, Cinquanta L, Corona O, Planeta D (2021) Microencapsulation of phenolic extracts from cocoa shells to enrich chocolate bars. Plant Foods Hum Nutr 76:449–457. https://doi.org/10.1007/s11130-021-00917-4
46. Grillo G, Boffa L, Binello A, Mantegna S, Cravotto G, Chemat F, Dizhbite T, Lauberte L, Telysheva G (2019) Cocoa bean shell waste valorisation; extraction from lab to pilot-scale cavitational reactors. Food Res Int 115:200–208. https://doi.org/10.1016/j.foodres.2018.08.057
47. Guirlanda CP, Alvim ID, Takahashi JA (2023) Atomization of cocoa honey using whey protein isolate to produce a dry formulation with improved shelf life for industrial application. Foods. https://doi.org/10.3390/foods12234269
48. Hasanuddin A, Anwar K, Mappatoba M, Hafsah (2019) Antibacterial and antioxidant activities of ethanol extracts of cocoa husk (Theobroma cacao L.) with Maltodextrine in Various Concentration. IOP Conf Ser: Earth Environ Sci 255(1). https://doi.org/10.1088/1755-1315/255/1/012017
49. Hashimoto JC, Lima JC, Celeghini RMS, Nogueira AB, Efraim P, Poppi RJ, Pallone JAL (2018) Quality control of commercial cocoa beans (*Theobroma cacao* L.) by near-infrared spectroscopy. Food Anal Methods 11(5):1510–1517. https://doi.org/10.1007/s12161-017-1137-2
50. Hernández-Hernández C, Viera-Alcaide I, Morales-Sillero AM, Fernández-Bolaños J, Rodríguez-Gutiérrez G (2018) Bioactive compounds in Mexican genotypes of cocoa cotyledon and husk. Food Chem 240:831–839. https://doi.org/10.1016/j.foodchem.2017.08.018
51. Hernández SMP, Estévez JJ, Giraldo LJL, Méndez CJM (2019) Supercritical extraction of bioactive compounds from cocoa husk: Study of the main parameters. Revista Facultad de Ingeniería 91:95–105. https://doi.org/10.17533/udea.redin.n91a09
52. Hernández Y, Costa-Bauza A, Calvó P, Benejam J, Sanchis P, Grases F (2020) Comparison of two dietary supplements for treatment of uric acid renal lithiasis: Citrate vs. citrate + theobromine. Nutrients 12(7):1–8. https://doi.org/10.3390/nu12072012
53. Herrero M, Mendiola JA, Cifuentes A, Ibáñez E (2010) Supercritical fluid extraction: recent advances and applications. J Chromatogr A 1217(16):2495–2511. https://doi.org/10.1016/j.chroma.2009.12.019
54. Huang Z, Shi XH, Jiang WJ (2012) Theoretical models for supercritical fluid extraction. J Chromatogr A 1250:2–26. https://doi.org/10.1016/j.chroma.2012.04.032
55. Huynh GH, Van Pham H, Hong Nguyen HV (2023) Effects of enzymatic and ultrasonic-assisted extraction of bioactive compounds from cocoa bean shells. J Food Meas Charact 17(5):4650–4660. https://doi.org/10.1007/s11694-023-01986-6
56. ICCO 2024 - Quarterly Bulletin of Cocoa Statistics - Production (2024) The International Cocoa Organization. https://www.icco.org/
57. Jafari S, Karami Z, Shiekh KA, Kijpatanasilp I, Worobo RW, Assatarakul K (2023) Ultrasound-assisted extraction of bioactive compounds from cocoa shell and their encapsulation in gum arabic and maltodextrin: a technology to produce functional food ingredients. Foods. https://doi.org/10.3390/foods12020412
58. Jakovljević M, Jokić S, Ačkar Đ, Molar M, Miškulin M, Palović N (2019) Green extraction techniques of bioactive components from cocoa shell. Croat J Food Sci Technol 11(1):11–20. https://doi.org/10.17508/cjfst.2019.11.1.02
59. Jang MH, Mukherjee S, Choi MJ, Kang NH, Pham HG, Yun JW (2020) Theobromine alleviates diet-induced obesity in mice via phosphodiesterase-4 inhibition. Eur J Nutr 59(8):3503–3516. https://doi.org/10.1007/s00394-020-02184-6
60. Janitschke D, Lauer AA, Bachmann CM, Winkler J, Griebsch LV, Pilz SM, Theiss EL, Grimm HS, Hartmann T, Grimm MOW (2022) Methylxanthines induce a change in the AD/neurodegeneration-linked lipid profile in neuroblastoma cells. Int J Mol Sci. https://doi.org/10.3390/ijms23042295
61. Jayaprakash P, Maudhuit A, Gaiani C, Desobry S (2023) Encapsulation of bioactive compounds using competitive emerging techniques: electrospraying, nano spray drying, and electrostatic spray drying. J Food Eng 339:111260. https://doi.org/10.1016/j.jfoodeng.2022.111260
62. Johannsen M, Brunner G (1994) Solubilities of the xanthines caffeine, theophylline and theobromine in supercritical carbon dioxide. Fluid Phase Equilib 95(8):215–226. https://doi.org/10.1016/0378-3812(94)80070-7
63. Jokić S, Gagić T, Knez E, Ubarić D, Kerget M (2018) Separation of active compounds from food by-product (Cocoa Shell) using subcritical water extraction. Molecules 23(6). https://doi.org/10.3390/molecules23061408
64. Jokić S, Nastić N, Vidović S, Flanjak I, Aladić K, Vladić J (2020) An approach to value cocoa bean by-product based on subcritical water extraction and spray drying using different carriers. Sustainability. https://doi.org/10.3390/su12062174
65. Jokić S, Pavlović N, Jozinović A, Ačkar Đ, Babić J, Šubarić D (2019) High-voltage electric discharge extraction of bioactive compounds from the cocoa bean shell. Chem Biochem Eng Q 33(2):271–280. https://doi.org/10.15255/CABEQ.2018.1525
66. Kentish S, Ashokkumar M (2011) In: Feng H, Barbosa-Canovas G, Weiss J (eds) Ultrasound Technologies for Food and Bioprocessing - The physical and chemical effects of ultrasound. Springer. https://doi.org/10.1007/978-1-4419-7472-3_1
67. Kentish S, Feng H (2014) Applications of power ultrasound in food processing. Annu Rev Food Sci Technol 5(1):263–284. https://doi.org/10.1146/annurev-food-030212-182537
68. Kumar K, Srivastav S, Sharanagat VS (2021) Ultrasound assisted extraction (UAE) of bioactive compounds from fruit and vegetable processing by-products: a review. Ultrason Sonochem 70:105325. https://doi.org/10.1016/j.ultsonch.2020.105325
69. Lanaud C, Vignes H, Utge J, Valette G, Rhoné B, Garcia Caputi M, Angarita Nieto NS, Fouet, O, Gaikwad N, Zarrillo S, Powis TG, Cyphers A, Valdez F, Olivera Nunez SQ, Speller C, Blake M, Valdez FJ, Raymond S, Rowe SM, … Argout, X. (2024). A revisited history of cocoa domestication in pre-Columbian times revealed by archaeogenomic approaches. Sci Rep 14(1). https://doi.org/10.1038/s41598-024-53010-6
70. Leadbeater NE (2014) In: Knochel P (Eds) Comprehensive Organic Synthesis - Organic Synthesis Using Microwave Heating. *2nd ed*. Elsevier Ltd. https://doi.org/10.1016/B978-0-08-097742-3.00920-4
71. Li Z, Fan Y, Xi J (2019) Recent advances in high voltage electric discharge extraction of bioactive ingredients from plant materials. Food Chem 277:246–260. https://doi.org/10.1016/j.foodchem.2018.10.119
72. Li Z, Jiang H, Xu C, Gu L (2015) A review: using nanoparticles to enhance absorption and bioavailability of phenolic phytochemicals. Food Hydrocolloids 43:153–164. https://doi.org/10.1016/j.foodhyd.2014.05.010

73. Llerena W, Samaniego I, Vallejo C, Arreaga A, Zhunio B, Coronel Z, Quiroz J, Angós I, Carrillo W (2023) Profile of bioactive components of cocoa (*Theobroma cacao* L.) by-products from Ecuador and evaluation of their antioxidant activity. Foods. https://doi.org/10.3390/foods12132583
74. Llompart M, Garcia-Jares C, Celeiro M, Dagnac T (2019) In: Worsfold P, Townshend A, Poole C, Miró M (eds) Encyclopedia of Analytical Science - Extraction | Microwave-Assisted Extraction, 3rd eds. Elsevier. https://doi.org/10.1016/B978-0-12-409547-2.14442-7
75. Malika M, Sonawane SS (2021) A Comprehensive review on the effect of various ultrasonication parameters on the stability of nanofluid. J Indian Assoc Environ Manag 41(4). http://op.niscair.res.in/index/php/JIAEM/index
76. Mandal SC, Mandal V, Das AK (2015) Classification of Extraction Methods. In Essentials of Botanical Extraction, Elsevier pp 83–136. https://doi.org/10.1016/b978-0-12-802325-9.00006-9
77. Mao Y, Robinson J, Binner E (2021) Understanding heat and mass transfer processes during microwave-assisted and conventional solvent extraction. Chem Eng Sci. https://doi.org/10.1016/j.ces.2020.116418
78. Maroun RG, Rajha HN, El Darra N, El Kantar S, Chacar S, Debs E, Vorobiev E, Louka N (2018) In: Galanakis C (ed) Polyphenols: Properties, Recovery, and Applications - Emerging technologies for the extraction of polyphenols from natural sources. Elsevier. https://doi.org/10.1016/B978-0-12-813572-3.00008-7
79. Mauricio López-Téllez J, del Pilar Cañizares-Macías M (2023) A paper-based analytical device with in-situ Carrez pretreatment for the determination of total polyphenolic content and antioxidant capacity. Food Chem 405. https://doi.org/10.1016/j.foodchem.2022.134952
80. Mazzutti S, Rodrigues LGG, Mezzomo N, Venturi V, Ferreira SRS (2018) Integrated green-based processes using supercritical CO_2 and pressurized ethanol applied to recover antioxidant compouds from cocoa (*Theobroma cacao*) bean hulls. J Supercrit Fluids 135:52–59. https://doi.org/10.1016/j.supflu.2017.12.039
81. Mellinas AC, Jiménez A, Garrigós MC (2020) Optimization of microwave-assisted extraction of cocoa bean shell waste and evaluation of its antioxidant, physicochemical and functional properties. LWT 127. https://doi.org/10.1016/j.lwt.2020.109361
82. MINAGRI (2023) Perú, centro de origen y productor mundial de cocoa orgánico. https://www.Gob.Pe/Institucion/Midagri/Noticias/841797-Peru-Centro-de-Origen-y-Productor-Mundial-de-Cocoa-Organico. Ministerio de Desarrollo Agrario y Riego, Perú
83. Mohamed RS, Saldaña MDA, Mazzafera P, Zetzl C, Brunner G (2002) Extraction of caffeine, theobromine, and cocoa butter from Brazilian cocoa beans using supercritical CO2 and ethane. Ind Eng Chem Res 41(26):6751–6758. https://doi.org/10.1021/ie0203936
84. Nayak N, Bhujle RR, Nanje-Gowda NA, Chakraborty S, Siliveru K, Subbiah J, Brennan C (2024) Advances in the novel and green-assisted techniques for extraction of bioactive compounds from millets: a comprehensive review. Heliyon 10(10):e30921. https://doi.org/10.1016/j.heliyon.2024.e30921
85. Nguyen VT, Nguyen NH (2017) Proximate composition, extraction, and purification of theobromine from cacao pod husk (*Theobroma cacao* L.). Technologies. https://doi.org/10.3390/technologies5020014
86. Nguyen VT, Huynh T, Tran N, Pham CA (2025) Utilization of cocoa pod husk (*Theobroma cacao* L.) for production of microencapsulated powder rich in alkaloids. Waste Biomass Valorization 16:459–470. https://doi.org/10.1007/s12649-024-02666-2
87. Nguyen VT, Tran AX, Le VAT (2021) Microencapsulation of phenolic-enriched extract from cocoa pod husk (*Theobroma cacao* L.). Powder Technol 386:136–143. https://doi.org/10.1016/j.powtec.2021.03.033
88. Okiyama DCG, Soares ID, Cuevas MS, Crevelin EJ, Moraes LAB, Melo MP, Oliveira AL, Rodrigues CEC (2018) Pressurized liquid extraction of flavanols and alkaloids from cocoa bean shell using ethanol as solvent. Food Res Int 114:20–29. https://doi.org/10.1016/j.foodres.2018.07.055
89. Pagliari S, Celano R, Rastrelli L, Sacco E, Arlati F, Labra M, Campone L (2022) Extraction of methylxanthines by pressurized hot water extraction from cocoa shell by-product as natural source of functional ingredient. LWT 170:114115. https://doi.org/10.1016/j.lwt.2022.114115
90. Pankaj SK, Wan Z, Keener KM (2018) Effects of cold plasma on food quality: a review. Foods 7(1):4. https://doi.org/10.3390/foods7010004
91. Parniakov O, Barba FJ, Grimi N, Lebovka N, Vorobiev E (2014) Impact of pulsed electric fields and high voltage electrical discharges on extraction of high-added value compounds from papaya peels. Food Res Int 65(Part C):337–343. https://doi.org/10.1016/j.foodres.2014.09.015
92. Pateiro M, Gómez B, Munekata PES, Barba FJ, Putnik P, Kovačević DB, Lorenzo JM (2021) Nanoencapsulation of promising bioactive compounds to improve their absorption, stability, functionality and the appearance of the final food products. Molecules 26(6):1547. https://doi.org/10.3390/molecules26061547
93. Pavlović N, Jokić S, Jakovljević M, Blažić M, Molnar M (2020) Green extraction methods for active compounds from food waste - cocoa bean shell. Foods. https://doi.org/10.3390/foods9020140
94. Pavlović N, Jakovljević M, Molnar M, Jokić S (2021) Ultrasound-assisted extraction of active compounds from cocoa bean shell. Food Health Dis Sci-Prof J Nutr Diet 10(2):77–88
95. Peralta-Jiménez L, Cañizares-Macías MP (2013) Ultrasound-assisted method for extraction of theobromine and caffeine from cocoa seeds and chocolate products. Food Bioprocess Technol 6(12):3522–3529. https://doi.org/10.1007/s11947-012-1014-3
96. Pereira-Caro G, Borges G, Nagai C, Jackson MC, Yokota T, Crozier A, Ashihara H (2013) Profiles of phenolic compounds and purine alkaloids during the development of seeds of *Theobroma cacao* cv. Trinitario. J Agric Food Chem 61(2):427–434. https://doi.org/10.1021/jf304397m
97. Pinelo M, Sineiro J, Núñez MJ (2006) Mass transfer during continuous solid-liquid extraction of antioxidants from grape byproducts. J Food Eng 77(1):57–63. https://doi.org/10.1016/j.jfoodeng.2005.06.021
98. Plaskova A, Mlcek J (2023) New insights of the application of water or ethanol-water plant extract rich in active compounds in food. Front Nutr. https://doi.org/10.3389/fnut.2023.1118761
99. Pudziuvelyte L, Marksa M, Sosnowska K, Winnicka K, Morkuniene R, Bernatoniene J (2020) Freeze-drying technique for microencapsulation of *elsholtzia ciliata* ethanolic extract using different coating materials. Molecules. https://doi.org/10.3390/molecules25092237
100. Ramirez Cabrera PA, Lozano Pérez AS, Guerrero Fajardo CA (2024) Innovative design of a continuous ultrasound bath for effective lignocellulosic biomass pretreatment based on a theorical method. Inventions. https://doi.org/10.3390/inventions9050105
101. Rasul MG (2018) Conventional extraction methods use in medicinal plants, their advantages and disadvantages. Int J Basic Sci Appl Comput 2(6):10–14
102. Rezvankhah A, Emam-Djomeh Z, Askari G (2020) Encapsulation and delivery of bioactive compounds using spray and freeze-drying techniques: A review. Dry Technol 38(1–2):235–258. https://doi.org/10.1080/07373937.2019.1653906
103. Riseh RS, Tamanadar E, Pour MM, Thakur VK (2022) Novel approaches for encapsulation of plant probiotic bacteria with sustainable polymer gums: application in the management of

pests and diseases. Adv Polym Technol 2022. https://doi.org/10.1155/2022/4419409
104. Rios-Aguirre S, Gil-Garzón MA (2021) Microencapsulación por secado por aspersión de compuestos bioactivos en diversas matrices: una revisión. Tecnológicas 24(51):e1836. https://doi.org/10.22430/22565337.1836
105. Rojo-Poveda O, Zeppa G, Ferrocino I, Stévigny C, Barbosa-Pereira L (2021) Chemometric classification of cocoa bean shells based on their polyphenolic profile determined by RP-HPLC-PDA analysis and spectrophotometric assays. Antioxidants. https://doi.org/10.3390/antiox10101533
106. Roobab U, Abida A, Madni GM, Ranjha MMAN, Zeng XA, Mousavi KA, Aadil RM (2023) An updated overview of ultrasound-based interventions on bioactive compounds and quality of fruit juices. J Agric Food Res 14:100864. https://doi.org/10.1016/j.jafr.2023.100864
107. Ruesgas-Ramón M, Suárez-Quiroz ML, González-Ríos O, Baréa B, Cazals G, Figueroa-Espinoza MC, Durand E (2020) Biomolecules extraction from coffee and cocoa by- and co-products using deep eutectic solvents. J Sci Food Agric 100(1):81–91. https://doi.org/10.1002/jsfa.9996
108. Rutkowska M, Namieśnik J, Konieczka P (2017) Ultrasound-assisted extraction. in the application of green solvents in separation processes, Elsevier Inc pp 301–324. https://doi.org/10.1016/B978-0-12-805297-6.00010-3
109. Saldaña MDA, Zetzl C, Mohamed RS, Brunner G (2002) Extraction of methylxanthines from guaraná seeds, maté leaves, and cocoa beans using supercritical carbon dioxide and ethanol. J Agric Food Chem 50(17):4820–4826. https://doi.org/10.1021/jf020128v
110. Sánchez M, Ferreira-Santos P, Gomes-Dias JS, Botelho C, Laca A, Rocha CMR (2023) Ohmic heating-based extraction of biocompounds from cocoa bean shell. Food Biosci 54. https://doi.org/10.1016/j.fbio.2023.102886
111. Sánchez M, Laca A, Laca A, Díaz M (2023) Cocoa bean shell: a by-product with high potential for nutritional and biotechnological applications. Antioxidants 12(5):1028. https://doi.org/10.3390/antiox12051028
112. Sanchez-Reinoso Z, Osorio C, Herrera A (2017) Effect of microencapsulation by spray drying on cocoa aroma compounds and physicochemical characterisation of microencapsulates. Powder Technol 318:110–119. https://doi.org/10.1016/j.powtec.2017.05.040
113. Taqi A, Farcot E, Robinson JP, Binner ER (2020) Understanding microwave heating in biomass-solvent systems. Chem Eng J. https://doi.org/10.1016/j.cej.2020.124741
114. Tavares IRG, Ramos Junior OJF, Souza MVG, de Oliveira GV, Alvares TS (2022) Development of a microencapsulated cocoa (Theobroma cacao) - based product and evaluation of total phenolic compounds and antioxidant capacity. Res Soc Dev 11(9):e2011931140. https://doi.org/10.33448/rsd-v11i9.31140
115. Thoo YY, Ng SY, Khoo MZ, Aida W, Ho CW (2013) A binary solvent extraction system for phenolic antioxidants and its application to the estimation of antioxidant capacity in Andrographis paniculata extracts. Int Food Res J 20(3)
116. Tiong TJ, Chu JK, Tan KW (2025) Advancements in acoustic cavitation modelling: progress, challenges, and future directions in sonochemical reactor design. Ultrasonics Sonochem 112. https://doi.org/10.1016/j.ultsonch.2024.107163
117. Tranquilino-Rodríguez E, Martínez-Flores HE, Rodiles-López JO, Martínez-Avila GCG (2021) Nanoencapsulation and identification of phenolic compounds by UPLC-Q/TOF-MS2of an antioxidant extract from *Opuntia atropes*. Funct Foods Health Dis 10(12):505–519. https://doi.org/10.31989/FFHD.V10I12.763
118. Uwineza PA, Waśkiewicz A (2020) Recent advances in supercritical fluid extraction of natural bioactive compounds from natural plant materials. Molecules 25(17):3847. https://doi.org/10.3390/molecules25173847
119. Vargas-Arana G, Merino-Zegarra C, Tang M, Pertino MW, Simirgiotis MJ (2022) UHPLC–MS characterization, and antioxidant and nutritional analysis of cocoa waste flours from the Peruvian Amazon. Antioxidants. https://doi.org/10.3390/antiox11030595
120. Versteeg FA, Picchioni F, Versteeg GF (2024) On the mass transfer of supercritical fluids, specifically super critical CO2: an overview. Chem Eng J. https://doi.org/10.1016/j.cej.2024.152521
121. Wrona O, Rafińska K, Możeński C, Buszewski B (2017) Supercritical fluid extraction of bioactive compounds from plant materials. In J of AOAC Int 100(6):1624–1635. https://doi.org/10.5740/jaoacint.17-0232
122. Yauri S, Fissore EN, Chavez SG, Rojas AM (2024) Advanced valorization of cocoa (Theobroma cacao L.) pod husks through 40 kHz-ultrasonic bath assisted extraction of pectins. Sustainable Chem Pharm 42. https://doi.org/10.1016/j.scp.2024.101869
123. Zabot GL, Schaefer Rodrigues F, Polano Ody L, Vinícius Tres M, Herrera E, Palacin H, Córdova-Ramos JS, Best I, Olivera-Montenegro L (2022) Encapsulation of bioactive compounds for food and agricultural applications. Polymers. https://doi.org/10.3390/polym14194194
124. Zabot GL, Viganó J, Silva EK (2021) Low-frequency ultrasound coupled with high-pressure technologies: impact of hybridized techniques on the recovery of phytochemical compounds. Molecules. https://doi.org/10.3390/molecules26175117
125. Zhang K, Li N, Wang Z, Feng D, Liu X, Zhou D, Li D (2024) Recent advances in the color of aquatic products: evaluation methods, discoloration mechanism, and protection technologies. Food Chem 434:137495. https://doi.org/10.1016/j.foodchem.2023.137495
126. Zainal B, Abdah M, Taufiq-Yap Y, Roslida A, Rosmin K (2014) Anticancer Agents from Non-Edible Parts of Theobroma cacao. Nat Prod Chem Res 2(4). https://doi.org/10.4172/2329-6836.1000134
127. Zainal-Abidin MH, Hayyan M, Hayyan A, Jayakumar NS (2017) New horizons in the extraction of bioactive compounds using deep eutectic solvents: a review. Anal Chim Acta 979:1–23. https://doi.org/10.1016/j.aca.2017.05.012
128. Zheng H, Zheng Y, Zhu J (2022) Recent developments in hydrodynamic cavitation reactors: cavitation mechanism, reactor design, and applications. Eng 19:180–198. https://doi.org/10.1016/j.eng.2022.04.027