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Review

Exploring the Feasibility of Cloud-Point Extraction for Bioactive Compound Recovery from Food Byproducts: A Review

Theodoros Chatzimitakos, Vassilis Athanasiadis, Martha Mantiniotou, Dimitrios Kalompatsios, Eleni Bozinou, Ioannis Giovanoudis and Stavros I. Lalas *

Department of Food Science and Nutrition, University of Thessaly, Terma N. Temponera Street, 43100 Karditsa, Greece; tchatzimitakos@uth.gr (T.C.); vaathanasiadis@uth.gr (V.A.); mmantiniotou@uth.gr (M.M.); dkalompatsios@uth.gr (D.K.); empozinou@uth.gr (E.B.); gio@uth.gr (I.G.)
* Correspondence: slalas@uth.gr; Tel.: +30-24410-64783

Abstract: In recent years, the production of food biomass waste has been increasing rapidly. This necessitates urgent measures to be taken so as to utilize them. Since most food biomass waste contains useful bioactive substances, cloud-point extraction (CPE) has emerged as a promising solution to valorize waste. CPE is an extraction method employed for the extraction and preconcentration of various chemical compounds, including polyphenols and flavonoids. As with any other extraction procedure, CPE isolates the target compound(s) from the sample, resulting in increased recovery. One major advantage of CPE is that the extraction is carried out without special equipment or harmful reagents. Moreover, other significant advantages are its effectiveness, simplicity, safety, and rapidity. This review focuses on the extraction of bioactive compounds from food-based waste using CPE and highlights the important parameters that can be tuned to improve the performance of CPE. Furthermore, the potential in promoting environmentally friendly practices within the food industry is also discussed.

Keywords: food biomass waste; cloud-point extraction; bioactive compounds; surfactant; temperature; pH; salting-out effect; recovery

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1. Introduction

Food biomass waste is an abundant, biodegradable organic resource produced worldwide. Food biomass waste constitutes about one-third of all food production and contributes to the greenhouse effect by producing greenhouse gases [1]. Therefore, food-biomass-waste valorization would not only minimize pollution, but it would also have the potential to generate biobased compounds, foods, and sustainable energy [2]. Food byproducts, for instance, have been valorized into biocomposites and bioplastics, as has the potential use of industrial biomass waste as an upcoming environmentally friendly energy source [3–7]. Zhang et al. [8] investigated energy and heat generation by food biomass waste using a mobile food-waste-to-energy system in conjunction with an anaerobic digester and a biogas engine. The bioconversion of waste food into insect-based protein growth for food or feed is one possible strategy to build a circular economy [9]. Furthermore, it is now usual to convert food waste into liquid biofuels [10–14]. As a result, the utilization of food-biomass-waste products is gaining popularity in the scientific, industrial, and government sectors [15]. Due to their technological, scientific, and economic benefits, conventional extraction techniques, such as Soxhlet extraction and hydrodistillation, have been used so far. Tavares et al. [16] employed hydrodistillation extraction to extract bioactive compounds from *Cymbopogon citratus* industrial waste. However, industries are shifting towards more environmentally friendly and efficient methods, able to extract bioactive compounds, such as flavonoids, polyphenols, carotenoids, phytosterols, and dithiones, that are found in foods. To this end, ultrasound-assisted extraction, microwave-assisted extraction, pressurized liquid extraction, solid–liquid extraction, liquid–liquid

extraction, and enzyme-assisted extraction are more and more being employed [17,18]. Enzyme-assisted extraction capitalizes on the selectivity of the enzymes to release bound bioactive compounds under mild conditions so as to preserve their biological activity [19]. Enzyme-assisted extraction has been employed to separate bioactive compounds from bay leaves [20], polyphenols from brocade orange peel [21], and banana peel [22]. Regarding microwave-assisted extraction, this method relies on the quick absorption of microwave radiation that is then transformed into heat and elevates the temperature via ionic conduction and dipole rotation. Microwave energy absorption, and consequently heat generation, can be evaluated using dissipation, implying that the presence of polar solvents is essential [23]. The benefits of this method include good repeatability and minimal sample treatment, as well as carrying out the extraction procedure by reducing the solvent volume, exposure time, and energy usage [24–26]. Several research groups have been interested in the extraction of pectin from food waste and byproducts using microwave-assisted extraction [27]. This method has been also employed to extract polyphenols from eucalyptus bark [28], peach byproducts [29], and cellulose from almond shell waste [24]. Solid–liquid extraction is a method that is based on transferring the desired compounds from the solid phase to the liquid-extractant phase, usually by employing organic solvents [30]. One major disadvantage of these methods is the potential degradation of the extracted compounds due to their light, temperature, and oxidation sensitivity [17]. This happens because high temperatures are incompatible with thermally sensitive substances, such as food bioactive vitamins, carotenoids, polyphenols, tocopherols, antioxidant molecules, and so on [31]. Another highly efficient extraction technique is pressurized liquid extraction, which occurs in a firmly sealed stainless-steel cell so that it can be exposed to both high-temperature and high-pressure conditions [32]. While the extraction procedure is on, the liquid phase is kept below its critical point. Pressure and temperature need to be determined to raise the rate of the mass transfer. This can be accomplished by lowering the surface tension, minimizing the viscosity of the solvent, and also by elevating the solubility of the components [18]. Pressurized liquid extraction has been utilized to isolate polyphenols from granadilla waste [33]. On the other hand, liquid–liquid extraction can also be used so as to partition the compounds from the aqueous phase into the immiscible, organic phase [30].

Cloud-point extraction (CPE), also known as the liquid-concentration technique, micelle extraction, or micelle-mediated extraction [34], is a highly efficient extraction method that exhibits specificity, simplicity, minimal solvent requirements, and applicability at low temperatures. Thus, CPE is a promising, environmentally friendly method that holds great promise in the extraction of food bioactive compounds efficiently [35]. CPE is one of the many methods known for recovering compounds from their matrices. These compounds can be either organic or inorganic, and are found in various foods. In the CPE method, the separation of compounds from the bulk solution occurs by the introduction of a surfactant, which leads to the formation of clouds (*vide infra*) when the solution is heated to or above a critical temperature, known as the cloud point. Surfactants used in CPE can either be ionic or nonionic. The separation of the desired compound from the bulk solution can also be enhanced by the addition of a salt via the salting-out effect [36–38]. Surfactants often accumulate at the interface between the hydrophilic (or aqueous) and the lipophilic phase, where the polar side is directed towards the aqueous part and the hydrophobic side is directed towards the lipophilic layer. Centrifugation is then applied to separate the solution into its two distinct phases. The structure of the micelles can range from roughly spherical to oval, depending on the type of surfactant and solution. The low requirements of CPE in reagents make it one of the most innovative technologies for extracting functional components. Moreover, CPE is typically accomplished at mild or low temperatures and without the use of hazardous or toxic reagents.

This review aims to provide a comprehensive assessment of CPE as a highly efficient extraction method for extracting bioactive compounds from food waste biomass. By exploring the principles, advantages, and recent applications of CPE, this review aims to highlight its significance in the valorization of food biomass waste. The review will

analyze the specific features that make CPE a promising and environmentally friendly method for extracting bioactive compounds efficiently. This review will contribute to a better understanding of CPE as an innovative technology promoting sustainable practices and generating value-added products.

2. Method Principle

2.1. Surfactants

Surfactants are substances that have the ability to reduce the surface or interfacial tension between various combinations of liquids, liquids and gases, or liquids and solids [39]. A surfactant is a substance that contains both hydrophobic and hydrophilic components, and when in low concentrations, adsorbs onto an interface or a surface and changes the free energy it has. Therefore, their amphiphilic nature makes them significant factors in chemical technology [40]. Emulsifiers, wetting agents, detergents, foaming agents, and dispersants are all examples of surfactants [39]. Their amphiphilic structures result in the existence of a part that is affine to the bulk solvent (polar part) and a part that is affine to a hydrophobic or lipophilic group. The hydrophobic tail is typically a hydrocarbon with six to twenty carbon atoms. This hydrocarbon can be either linear or branched, and it might even have aromatic rings, whereas the surfactant head group might be ionic or nonionic. Surfactants are divided into four categories based on the hydrophilic group they have (Table 1) [41]. One of the most notable characteristics of surfactants is their excellent capacity to dissolve certain molecules through electrostatic, hydrophobic, or a combination of the two. Another distinguishing property is that, when heated, the micellar solution turns opaque across a narrow temperature range, known as the cloud-point temperature [42]. The solution separates into two distinct phases when the temperature rises above the cloud point: a surfactant-rich phase and an aqueous phase. Due to the tiny amount of the surfactant-rich phase, an excessive enrichment factor can be produced [43]. This results in the increased sensitivity of the analysis without the need for additional sample cleaning or evaporation processes [44].

Table 1. The four categories of surfactants used in CPE.

Category	Properties	Example
Nonionic	The hydrophilic head is uncharged	Polyoxyethylenes (Genapol X-080, Triton X-100, Tween 80)
Anionic	The hydrophilic group contains an anionic moiety, such as carboxylate, sulfonate, or sulfate	Sodium dodecyl sulfate, ammonium lauryl sulfate, sodium laureth sulfate
Cationic	The hydrophilic head contains positive groups, such as quaternary ammonium	Cetyl trimethylammonium bromide, methylbenzethonium, benzalkonium
Zwitter anionic	cationic, anionic, or neutral, depending on the solution's pH	4-(Dodecyldimethyl ammonium) butyrate, erucyl amidopropyl betaine

The optimal critical micelle concentration (CMC) plays a crucial role in the method of CPE, so phase separation can occur only within a limited concentration range. Excessive use of surfactant seems to decrease the extraction efficiency, owing to a reduction in the preconcentration factor. Conversely, a smaller quantity of surfactant results in inadequate analyte recovery [45].

2.2. Micelle Formation

For CPE, the formation of micelles is of outmost importance. In the case of nonionic surfactants, micelles are formed when the solution is heated to a temperature above the cloud point of the surfactant used. The temperature in which micelles are formed is also known as the Krafft temperature (*vide infra*). The cloud point is the temperature at which a surfactant solution produces a coacervate, splitting into two phases: the surfactant-rich coacervate and a second phase with a low surfactant concentration [46]. The target compound concentration in the coacervate is also possible because this phase has a lesser volume than

the surfactant-depleted phase [45–47]. Thus, by merely adjusting the system temperature, the extracted compounds entrapped in the micelles can be concentrated [46,48]. When the surfactant concentration exceeds a particular threshold (i.e., CMC), the surfactant molecules become tightly associated and form colloidal-sized molecular aggregates. These micelles, which contain between 60 and 100 monomers, are at equilibrium with a surfactant concentration in the solution near the CMC. Other forms, such as inverse micelles, microemulsions, vesicles, monolayers, and bilayers, may form depending on the composition and concentration of the surfactant, as well as the solvent utilized [36]. Because the surfactant exists as a monomer, it easily reaches the CMC, and the molecules begin to form micelles. The hydrophobic tails of the micelles are oriented to the interior to avoid their interaction with water, while the hydrophilic heads approach and orient towards the water molecules on the outer surface [41]. In many cases, micelle formation is promoted through the addition of a salt, such as sodium sulfate or sodium chloride, which is known as the salting-out effect. The process of micellization in ionic and amphoteric surfactants is influenced by temperature due to alterations in the hydrophobic and head-group interactions. In the context of an aqueous solution, the CMC of ionic surfactants exhibits a monotonically decreasing trend as the temperature increases, reaching a minimum at approximately 25 °C. However, beyond this point, the CMC starts to increase as the temperature continues to rise, demonstrating a U-shaped behavior [49]. On the other hand, the CMC of nonionic surfactants exhibits a decrease with the increasing temperature. The process of dissolution in water involves the formation of hydrogen bonds between the hydrophilic head of the substance, typically an ethylene oxide chain, and water molecules. The bonding strength of a solution can be compromised by an elevation in thermal energy, resulting in a temperature-dependent turbidity due to the dehydration of ethylene oxide units and the subsequent aggregation of micelles [50]. Micelles can take on a variety of shapes, ranging from almost spherical to oval, depending on the type of surfactant used and the conditions of the solution. The method through which extraction happens is still unknown [51]. When the micelles are formed, the hydrophilic and the lipophilic phases are separated by centrifugation. The lipophilic phase is the one that is the surfactant-loaded phase because it consists of the majority of the surfactant molecules as well as the hydrophobic molecules already existing in the solution. The aqueous phase includes all molecules or ions that cannot be merged into the micellar system. The number of surfactant molecules within a micelle is referred to as the degree of aggregation. The micelle number can be affected by the surfactant type, the group structure, the properties of the electrolyte, the concentration, the solvent nature, the temperature, and the pH of the solution [31,52]. Figure 1 illustrates the mechanism of the micelle formation when nonionic surfactants are applied.

2.3. pH Level of the Solution

The pH of the medium is a crucial factor that has a major effect on the CPE, particularly for ionizable compounds. Optimizing the pH of these compounds can potentially improve the recovery of the analyte by decreasing its solubility in the aqueous phase [53]. The protonation/deprotonation of compounds results in an electrically neutral charge. These compounds typically exhibit a negligible reaction towards the micellar aggregate, as the analytes tend to distribute into the micellar phase of the nonionic surfactant [54]. Consequently, the quantitative extraction method occurs at pH levels in which the neutral state of the analyte predominates.

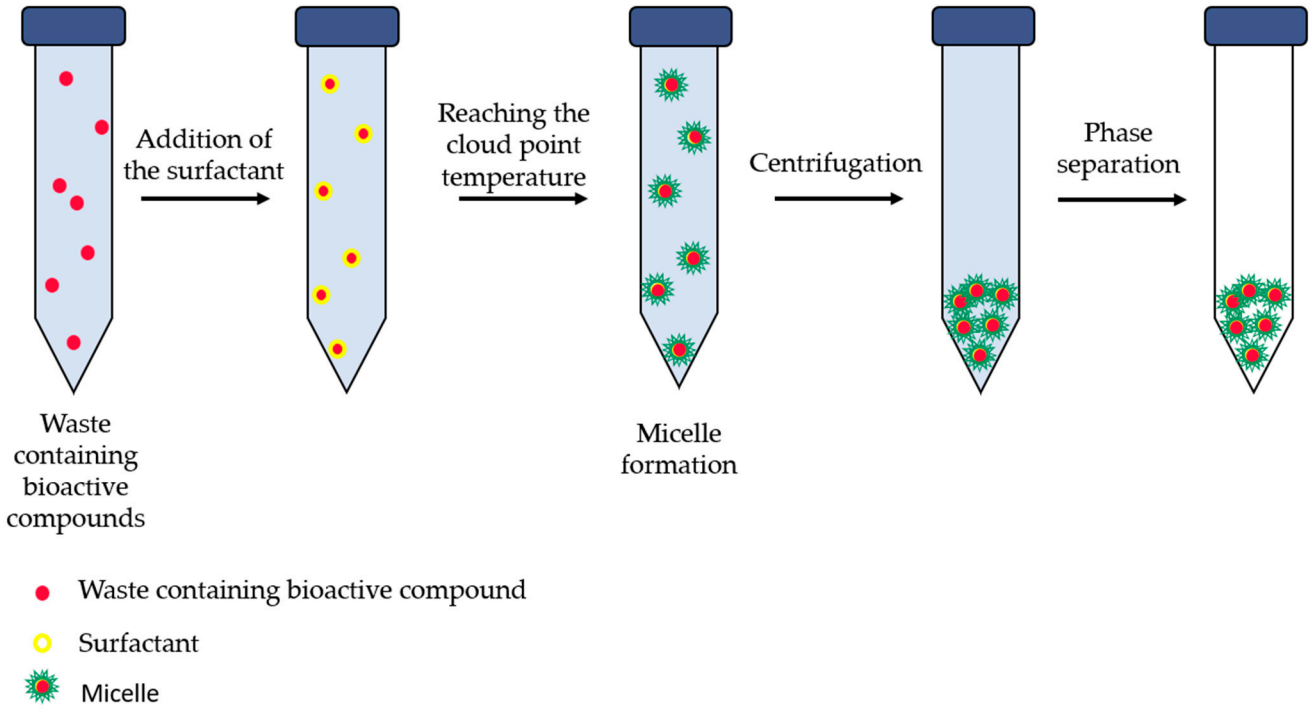

Figure 1. The mechanism of the CPE method when a nonionic surfactant is utilized.

2.4. Salting-Out Effect

One very important parameter that can enhance the CPE method is the salting-out effect. The salting-out effect occurs when a relatively high concentration of the electrolyte is present and causes the nonelectrolyte to become less soluble. By increasing the dehydration level of micelles, the addition of salt to a micellar solution enhances hydrophobic interactions between them. Turbidity arises when the surfactant concentration is excessively high. At that moment, phase separation is possible. The utilization of the salting-out effect in CPE prevents the heating phase, shortening the separation time.

The presence of salts may influence the CMC value. In situations where the surfactant is nonionic, the presence of an electrolyte results in a reduction of the CMC and a subsequent decrease in the separation efficiency [55]. Ionic surfactants are known to enhance the ionic strength of a solution, thereby expediting phase separation through the enhancement of the water-phase density [56]. The presence of electrolytes enhances the efficacy of the extraction method for polar compounds. The utilization of this particular technique results in a decrease in the critical packing temperature and enhances the efficacy of hydrophobic interactions that occur between the surfactant and the analyte [57].

2.5. Temperature

Temperature is another significant factor affecting the CPE method. It is recommended that the temperature for extraction should be elevated by approximately 15–20 °C compared to the cloud point of the surfactant. The Krafft point refers to the temperature at which the solubility of the surfactant experiences a significant increase in an aqueous solution. This occurrence is commonly understood as the melting point of a hydrated solid surfactant. Application of the Krafft point has been widely employed in ionic surfactants, while in nonionic surfactants has been scarcely recorded [58]. These are illustrated in detail in Figure 2. Raising the temperature of the solution over the surfactant's cloud point leads to the dehydration of the micelles and the production of a turbid solution, resulting in phase separation [47]. Elevating the equilibrium temperature results in a reduction of the volume of the surfactant-rich phase due to the decreased interruption of hydrogen bonds and dehydration of the phase [59]. This results in a boost in the extraction yield [60]. Nonetheless, the recovery of the analyte may be hindered by elevated temperatures, as

thermolabile compounds may undergo decomposition. Temperatures ranging from 40 to 60 °C are commonly employed [59].

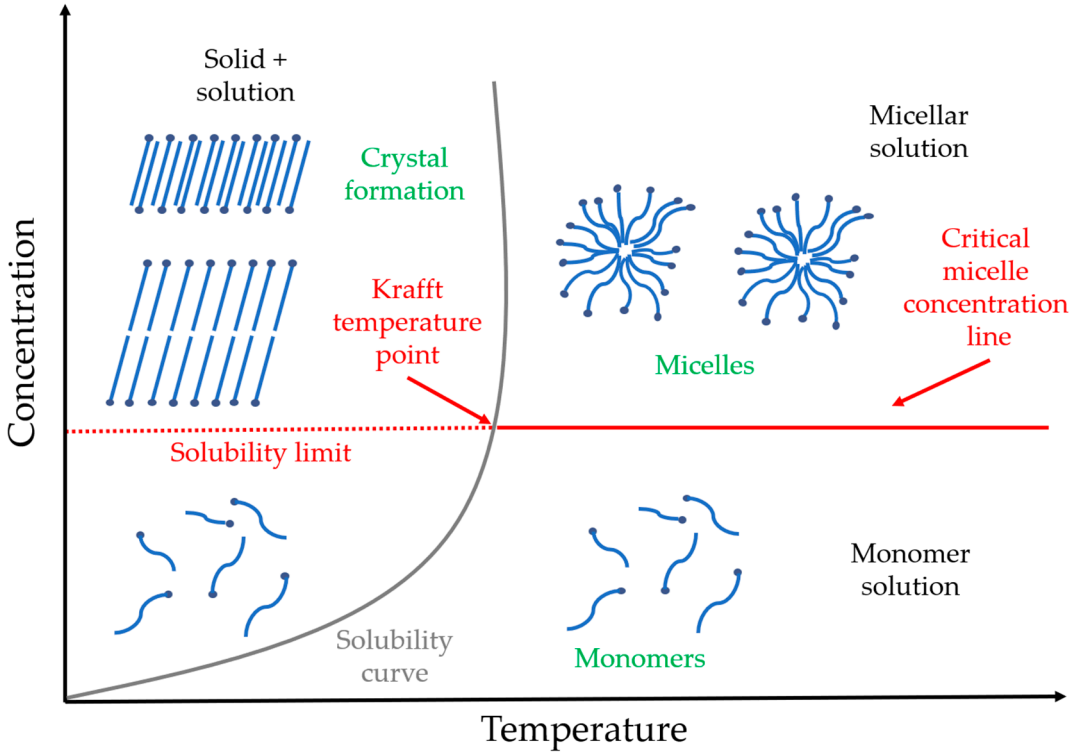

Figure 2. Effects of the CMC and Krafft temperature of ionic surfactants in aqueous solutions.

3. Application of CPE for Bioactive Compound Extraction in Food Byproducts

3.1. Olive-Based Waste

Olive tree harvesting is expanding globally, resulting in a large amount of waste. Olive leaves (20–25% by weight) are produced initially during tree pruning, and then in mill leaves and thin branches (olive mill leaves) [61]. Since the global demand for olive oil has increased, the olive processing industry has generated a large amount of agroindustrial wastewater. Olive mill wastewater (OMW) residues consist of both solid waste (olive pulp) and liquid waste (vegetables and additional water generated during decantation). OMW has a dark-brown (often black) color and a strong, pungent perfume reminiscent of olives [62]. Additionally, table olive processing involves many procedures that generate several waste streams: lyes, washing wastewaters, brines, and machine washwaters [63]. Large volumes of olive mill effluent are generated during the continuous three-phase olive-oil-extraction method, causing major environmental issues [64]. The valorization of such wastes is of great importance, both for the environment and food technology, as natural polyphenolic antioxidants from agricultural wastes are gaining great interest [65].

Kiai et al. [63] examined the applicability of CPE using three different nonionic surfactants, Genapol X-080, Triton X-100, and Tween 80, for the extraction of polyphenols from table OMW. The optimal conditions for the CPE of polyphenols were investigated in relation to various experimental parameters, including the surfactant content, solution pH, equilibrium temperature, and incubation period. The optimum conditions were defined as 10% surfactant (*w*/*v*), with a pH of 2, at 70 °C, and an equilibration time of 30 min. It was found that Triton X-100 and Tween 80 had a higher recovery for the polyphenols than Genapol X-080. This is reasonable, considering that Triton X-100 and Tween 80 have a similar chemical structure, as they are both nonionic polyethylene oxide emulsifiers. Genapol X-080 is a nonionic emulsifier that consists of acrylates. The recovery rate of hydroxytyrosol was nearly identical for all three surfactants. Furthermore, Tween 80 demonstrated the

capability of extracting caffeic acid with a recovery ratio of 75.5%, in addition to the other two surfactants that showed lower recoveries. Katsoyannos et al. [65] investigated the yield of polyphenols isolated from OMW using Triton X-114. Triton X-114 is also nonionic and an excellent surfactant choice, as it requires low temperatures, and it has good detergent and wetting characteristics. The results of their study revealed that the best conditions are a three-step CPE with 2% Triton X-114 at 55–60 °C for 20 min. When a three-step CPE is used with 2% v/v surfactant in each step, a total surfactant volume of 6% of the sample volume is required to separate more than 90% of the polyphenols from the aqueous phase. Multiple extraction procedures should be employed to achieve >90% recoveries. Moreover, it is shown that CPE can be effectively applied to aqueous polyphenolic solutions and, when fatty substances are absent, polyphenols can be quantitatively extracted. Comparing these two studies, it is obvious that Triton X-114 is a more favorable surfactant than Triton X-100. This stems from the fact that it can achieve higher recoveries in lower temperatures and with a lower surfactant concentration. Nevertheless, these conditions are only applicable to the extraction of polyphenols. Next, Gortzi et al. [51] evaluated Genapol X-080 as a CPE surfactant for the separation of polyphenols and tocopherols from OMW and measured the recovery values. The results showed that the recovery of polyphenols was proportionate to the percentage of Genapol X-080 and that the recovery of tocopherols was quantitative even when the concentration of Genapol X-080 was only 5% w/v, and the equilibrium temperature was 55 °C for 20 min. When multistep CPE was applied, higher yields were achieved, which is in line with Kiai et al. [63]. In another study, Katsoyannos et al. [66] evaluated the possibility of applying CPE on OMW utilizing low-biohazard surfactants. In this category, surfactants such as Tween 20, Tween 80, Span 20, and PEG 400 were used. All these surfactants are also nonionic, and they were used in the separation of natural antioxidants, polyphenols, and carotenoids present in OMW and red-fleshed orange juice. Among the selected surfactants, Tween 80 was found to be the most appropriate for both OMW and red-fleshed orange juice, at a concentration of 5% w/v and 7% w/v, respectively. The equilibrium temperature was 55 °C and the equilibrium time was 30 min. All other surfactants provided low recoveries. Optimization of experimental CPE parameters would improve extraction efficiency and could provide the basis for more the cost-effective isolation of antioxidants from natural sources. Athanasiadis et al. [62] extracted the polyphenols from OMW by using CPE with lecithin, a common emulsifier, as a surfactant, and the extracted polyphenols were exploited to enrich olive oil. Lecithin is a zwitter anionic surfactant and it can be produced in animal and plant tissues. It is nontoxic and edible. The CPE extraction procedure took place for 20 min at 40 °C and with a pH of 3.5, and the concentration of the emulsifier was 3% w/w. The lecithin emulsifier resulted in a recovery of up to 42.2%. The concentration of total polyphenols in olive oil samples increased with the addition of micellar dispersions. This increase led to a considerable reduction in free radicals in this sample when compared to other samples. The colors of the samples were consistently maintained, there was no visible sediment, and the flavor of the olive oil was delicious and delightful. This study showcases the applicability of the extracts obtained by CPE and their advantages. Because further study was necessary to maximize the extraction of polyphenols from OMW, Karadag et al. [67] analyzed the effect of the extraction temperature, pH, sodium chloride, lecithin concentration, and equilibration time on the recovery of polyphenols using single-factorial experiments and the optimization of these parameters by response-surface analysis. They concluded that the high recovery of total polyphenols from OMW was achieved by utilizing lecithin in the CPE method under the method conditions optimized by the response-surface methodology. The optimum parameters were established to be 80 °C, with a pH of 5.5, a 20% w/v sodium chloride concentration, and a 12.5% w/v for lecithin. As the equilibration time did not affect the recovery of polyphenols, it was excluded from the optimization study. The higher oxidative stability of this OMW-enriched lecithin was confirmed in a salad dressing sample. According to these results, lecithin is not as good as Tween 80 for the extraction of polyphenols, as it had lower recoveries even when higher concentrations were employed. El-Abbassi

et al. [64] used the CPE method to extract polyphenols from an ultrafiltered sample of OMW. The ultrafiltration minimized the organic load and suspended solids, and a more clarified OMW was produced. This clarified extract had easy phase visualization during the cloud-point extraction, while it could keep the total polyphenol content as high as possible. Response-surface methodology was used to optimize the yield of polyphenols from OMW using Triton X-100 as a surfactant. The proper conditions were found to be a one-step CPE using 10% of Triton X-100 at 90 °C for 30 min. CPE using Triton X-100 was successfully employed for OMW, resulting in a quantitative phenol extraction, with a yield of 66.5%. Up until now, the most efficient way to extract bioactive compounds from OMW appears to be a multistep CPE, and the most appropriate surfactant appears to be Triton X-114 for the polyphenols and Genapol X-080 for tocopherols. A notable advantage of CPE is its minimal surfactant consumption on an industrial scale compared to other conventional extraction techniques. Additionally, the unique potential to directly incorporate the extract into food is of high importance. The superiority of CPE is further demonstrated in the following study conducted by De Marco et al. [68]. This study involved the implementation of liquid–liquid extraction, wherein equal volumes of OMW were mixed with solvents, such as hexane or ethyl acetate. In spite of the promising results, this approach required a significant solvent consumption and mainly lacked the direct applicability in food.

Stamatopoulos et al. [69] proposed a rapid, clean, energy-efficient, and nontoxic method for the extraction of oleuropein and related polyphenols from olive leaf extract using cloud-point extraction (CPE) assisted by the salting-out effect. In these methods, Tween 80 was selected as a surfactant. Oleuropein and related polyphenols were heated to improve their thermal stability. The principle of the method relied on increasing the sulfate concentration, capitalizing on the salting-out effect, followed by the separation of the enriched phase from the bulk solution through centrifugation. This method not only facilitated the phase separation but also contributed to the reduction in the solubility of polyphenols. The method also helped to lower the cloud-point temperature of Tween 80. Optimal conditions were selected as a pH of 2.6, an ambient temperature of 25 °C, 4% Tween 80 (w/v), 35% sodium sulfate (w/v), and a settling time of 5 min. The total recoveries of oleuropein and the rest of the polyphenols were between 93 and 100%. In comparison, the polyphenols that remained in the surfactant-rich phase displayed higher thermal stability.

3.2. Wine-Based Waste

Winemaking generates a huge amount of waste, mostly known as wine sludge. Wine sludge is defined as any residue left in wine containers after fermentation, storage, and processing, plus whatever remains after the filtering and/or centrifugation of the wine product [70]. Despite their polluting nature, grapes, wine, grape seeds, and skin extracts have been shown to have beneficial effects on human health, such as protection against cardiovascular disease, anti-inflammatory activity, and anticarcinogenic effects, due to their high content of polyphenols [71].

Chatzilazarou et al. [71] were the first to investigate the CPE method in the wastes from the wine industry. They intended on isolating polyphenols from wine sludge waste. A double-step CPE method was performed at the optimal conditions with 5% PEG 8000 or 2% Genapol X-080 in each CPE stage. The optimal conditions were used for each surfactant. In the case of PEG 8000, these were a pH of 2.5 and heating at 55 °C for 30 min. When it came to Genapol X-080, the optimal conditions were a pH value of 3.5, a temperature of 55 °C, and 30 min of equilibration. The extraction of the polyphenols yielded 75.8% in the double-step CPE with total consumption of 4% of Genapol X-080, and in the case of PEG 8000, the yield was 98.5% with a general consumption of 10%. The use of PEG 8000 led to a higher polyphenol yield. The acidic conditions applied during the CPE method may have been a beneficial factor in this. However, in the two CPE steps, the total consumption of Genapol X-080 was much lower than that of PEG 8000. For this purpose, it would be worthwhile to repeat these experiments under the same conditions, but with three CPE

steps applied. In this way, it could be assessed whether having three CPE steps and using Genapol X-080 would lead to a higher recovery of polyphenols with a lower consumption of the surfactant. Alibade et al. [70] employed CPE for the extraction of polyphenols from wine sludge. They used lecithin as a surfactant and they investigated the optimum conditions for the method. Lecithin was chosen as a surfactant in this investigation since it is an edible, harmless substance that is also quite inexpensive. Furthermore, there is no need to separate recovered polyphenols from the surfactant environment before incorporating them into foods. To obtain that, they implemented multiple extraction steps, varying from one to three. Then, they tested the temperature between 35 and 55 °C and the pH value from 2.5 up to 5.0. They also used four different concentrations of the surfactant, more specifically 2, 5, 10, and 15%, to examine which one provided better conditions for the extraction. The method was then optimized as 5% lecithin concentration, at 40 °C, and with a pH of 3 for a 30 min equilibrium time. Three steps of CPE were employed. When the method was finished, a high recovery of polyphenols was achieved, up to 76%. Similarly, to the application of lecithin as a surfactant in the olive mill waste, as in the case of wine sludge, the use of an emulsifier is not as effective as the conventional surfactants.

The simplicity and swiftness of the CPE technique compared to other techniques is worth noting. A research study conducted by Brianceau et al. [72] evaluated a novel methodology for the utilization of fermented grape pomace through the application of a pulsed electric field. Following the implementation of the pulsed-electric-field treatment, the extraction of polyphenols from grape pomace was conducted in a cylindrical extraction cell using a mixture consisting of 50% ethanol v/v at a temperature of 50 °C, with the ratio of liquid to solid being consistently maintained at a value of 5. The combination of densification and the pulsed-electric-field treatment demonstrated significant efficacy in augmenting the extraction of total anthocyanins (~0.57 g/100 g of raw material) from fermented red-grape pomace, thereby establishing its industrial relevance. The application of the pulsed-electric-field treatment on fermented-grape pomace enables the targeted extraction of total anthocyanins across a spectrum of temperatures. Therefore, this technique has the potential to serve as a substitute for traditional methods of preparing raw materials, such as dehydration and grinding. These conventional pretreatment techniques not only have negative effects on the quality of the final product, but also require a significant amount of energy. However, when handling large amounts of wine waste, the pulsed electric field seems more laborious than CPE, making it a challenging task to handle.

3.3. Pomegranate-Based Waste

Pomegranate fruit is divided into three parts: juice, seeds, and peels. Pomegranate contains a high concentration of bioactive components, such as organic acids, polyphenols, and flavonoids. Despite its high concentration of beneficial components, this fruit has 60% waste in the form of peels. Pomegranate peels have a high concentration of bioactive compounds, such as polyphenols, flavonoids, and organic acids. Because of their multifunctional, high nutritional, and bioactive properties, peels have recently been used in the food, pharmaceutical, and chemical processing industries [35,73].

Pomegranates are known to have high amounts of bioactive compounds. Pomegranate peel waste was studied by Motikar et al. [35]. At first, a series of experiments was carried out so as to choose the best method and the optimum parameters for the extraction of the bioactive compounds, such as polyphenols and flavonoids, from the peel waste. The methods examined were conventional extraction, ultrasound extraction, microwave extraction, ultrasound-assisted CPE, and microwave-assisted CPE. Next, they followed another series of tests so they could optimize the conditions of the CPE method. They tested four different surfactants, Triton X-100, Triton X-114, Tween-20, and Tween-80. The most suitable one was chosen (i.e., Triton X-100) because of its high density, which makes phase separation by centrifugation feasible. Then, they investigated the surfactant concentration that was necessary for the maximum recovery of the bioactive compounds. Afterwards, the solid–liquid mixing ratio was tested, along with the pH value. A range of temperatures

and equilibration time experiments followed, where the tested temperature values were between 35 and 80 °C and the tested equilibrium times were between 20 and 60 min. Finally, the salt concentration that would lead to the maximum recovery of bioactive compounds was investigated. The tested sodium chloride concentrations were between 6 and 18% w/v. The surfactant concentration of 2% v/v was insufficient for further phase separation, while at 10% v/v, the phase was too viscous, resulting in no micelle formation. Because the extraction yield is affected by the mass-transfer phenomenon, the solid-to-liquid ratio was investigated. The larger the concentration gradient between solution and solvent, the greater the mass transfer and, consequently, the extraction yield. In terms of the pH, at low pH values, the polyphenols are protonated, resulting in hydrophobic molecules that interact more strongly with hydrophobic micellar surfactant, and therefore easily become trapped in the micelles. On the other hand, the polyphenols are deprotonated and their ionic properties rise at high pH values, resulting in a decrease in the solubility of the hydrophobic polyphenols in the micelles due to increased proton activity. The equilibrium temperature may influence the time it takes for organic molecules and surfactant micelles to form. The extraction efficiency decreased as the incubation time was beyond 30 min; the stability of the polyphenols due to degradation may occur if the sample is retained for a longer time at a higher temperature up to 60 min. The frequency of ultrasonication is an important component in tissue disruption. As a result, the effect of ultrasonication combined with cloud-point extraction on polyphenol recovery was tested. The maximum recovery was achieved when the ultrasound-assisted CPE was followed, with a ratio of 1 to 70 pomegranate peel powder to the solvent used. The extraction solvent was 70% ethanol in water. The surfactant utilized was Triton X-110 at a content of 8% v/v. The optimum temperature was 55 °C, at an acidic of pH value 4.5, and the method was performed for 30 min. Furthermore, sodium chloride at a content of 14% was added so the salting-out effect would be provoked. The total polyphenol and flavonoid recovery were expressed as antioxidant activity. The greatest antioxidant activity was calculated to be 94.48%. Next, Sun et al. [73] worked on the optimization of this method. To do so, the response-surface methodology was employed. The maximum recovery was obtained when the optimal parameters were established. So, a solid-to-liquid ratio of 1:40 g/mL was applied. The most suitable surfactant was found to be Triton X-100 at a content of 10% (v/v), and the optimum sodium chloride concentration was 14% (w/v). The pH value was 4.0. All these parameters were applied for 40 min at 65 °C. The yield of the bioactive was up to 82.37 mg GAE/g. This result enhanced the applicability of CPE on pomegranate peel waste, in order to valorize the bioactive compound existing in them.

In a study conducted by Živković et al. [74], the most favorable parameters for the ultrasound-assisted extraction of polyphenols from pomegranate peel were examined through the utilization of the response-surface methodology. These conditions included 25 min of extraction at an 80 °C extraction temperature, a 59% ethanol concentration, and a 1:44 solid to solvent ratio. Despite the satisfactory recovery of polyphenols (~149 mg GAE/g dw) and the low procedure time, the large amounts needed for extraction make it difficult to manage large amounts of waste.

3.4. Berry-Based Waste

De Araújo Padilha et al. [75] evaluated the polyphenol recovery from camu-camu (*Myrciaria dubia* McVaugh). Camu-camu is a red berry, typically found in South America, near the Amazon River. Its residue has been discovered to retain bioactive constituents, which may have anticancer activity [76,77]. That is why the research team decided to explore the content of the bioactive compound by implementing CPE. The surfactant they exploited was Triton X-114. The surfactant was studied at various concentrations, between 1 and 10 wt%. The equilibrium temperatures tested were between 30 and 60 °C. The most appropriate pH value for the extraction was also investigated. The tested pH values were between 2 and 10, from a strongly acidic environment to an alkalic environment. Furthermore, sodium chloride was added, and its optimal concentration was also studied.

A series from 0 to 10 wt% sodium chloride was tested. It was noticed that the addition of salt to the system significantly inhibited the polyphenol recovery. Thus, a CPE method was employed with the adjusted parameters. The system was constituted by an 80 wt% camu-camu extract, 7 wt% Triton X-114, and sodium chloride, without adjusting the pH value. The method of extraction took place at 30 °C for 3 h, and the total polyphenol recovery that was obtained was up to 95.71%. Despite significantly decreasing the method efficiency, the salting-out effect induced by the sodium chloride addition enabled a larger concentration of polyphenols in the coacervate phase due to the reduced volumetric ratio.

Na Guo et al. [78] developed a methodology for the simultaneous extraction and analysis of five target bioactive compounds in mulberry leaf samples. The five desired bioactive compounds were deoxy-nojirimycin, chlorogenic acid, rutin, isoquercitrin, and astragalin. The method they applied was an ultrasonic-assisted cloud-point extraction with aqueous solutions of surfactants for extraction and preconcentration. Then, the five target substances were determined by reversed-phased high-performance liquid chromatography. The research team investigated the optimum conditions. They established an acidic CPE system for the extraction, modifying the surfactant Triton X-114 by adding hydrochloric acid to it. Firstly, they tested the effect of the surfactant concentration. A range from 1 to 5% was tested, and 3% of the surfactant was found to be the one that demonstrated the maximum recovery. As for the pH value, it was kept lower than the pKa values of the analyzed polyphenols, which helped their extraction. Afterwards, a response-surface methodology was applied in order to optimize the extraction method. The results showed that the improved Triton X-114 system should include 0.05 M hydrochloric acid and 3% Triton X-114. A 35:1 liquid–solid ratio, a 45 min ultrasonic runtime at 25 °C, and a 360 W ultrasonic power were found to be the ideal ultrasonic-assisted CPE conditions. The temperature was raised during the separation studies, which resulted in an average transfer efficiency of 89.2% for polyphenols and 85.9% for alkaloids in the bottom and top phases.

The feasibility of the direct administration of the extract into food could be further demonstrated by the following study conducted by Cunha-Santos et al. [79], where camu-camu byproducts were valorized by the use of conventional extraction. The concentrations of total phenolic compounds in camu-camu were found to be highest in both the seed and pulp, in comparison to the peels of the fruit. The results showed that the optimal solvent composition for extracting phenolic compounds from camu-camu peels and pulps was determined to be aqueous ethanol (80%, v/v), while aqueous methanol (50%, v/v) was selected for the seed. However, there are concerns about the extracts' use in the food industry.

3.5. Other Food-Based Waste

Giovanoudis et al. [80] studied and optimized the recovery of the carotenoids from tomato-liquid waste samples. They implemented a CPE method with food-grade lecithin as the surfactant. Additionally, factors influencing the extraction, such as the ionic strength, sample pH, extraction temperature, and surfactant concentration, were investigated and adjusted. Among a variety of 1% up to 35.6% of sodium chloride, 35.6% was found to lead to the maximum yield of the carotenoids. Different pH values, ranging from 2.5 to 8 were also tested. As for the temperature equilibrium, a series of experiments were conducted, with temperatures varying between 20 and 65 °C. Next, the effect of the surfactant concentration and the possibility of a multiple-step CPE were examined. They experimented with three steps of CPE with 1 and 2% of lecithin. The optimized method was revealed to be either a two-step CPE with 2% of the surfactant, or a three-step CPE with a 1% surfactant concentration. The maximum carotenoid yield was achieved when the pH value was adjusted to 3.5, the temperature was set at 45 °C, and the equilibrium time was 20 min. The addition of 35.6% w/v sodium chloride was necessary to provoke the salting-out effect and maximize the recovery of the bioactive compounds. The antioxidant activity of the carotenoids extracted using the optimized approach was 36.3%, which was 10 times lower than the initial samples. This result indicates that the extracted compounds remain

active. Further clarification on the possibility of use in the food industry is possible with the following work. The utilization of high-hydrostatic-pressure extraction was studied by Grassino et al. [81], and has been determined to be a suitable method for the extraction of polyphenols from tomato peel waste, as it allows for a high recovery rate while requiring a minimal time investment of only 5 min. Different combinations of parameters were utilized to achieve the isolation of varying quantities of phenolic compounds. The most optimal extraction efficiency was observed when both 50 and 70% methanol were combined at temperatures of 45 and 55 °C. However, the utilization of this product is hindered by its lack of compliance with food-grade standards, as stated by the authors.

The same research team, Giovanoudis et al. [82], applied the CPE method to separate natural antioxidants, and more specifically polyphenols, from apricot cannery waste. They examined the concentration of food-grade surfactants, such as lecithin, PEG 8000, Genapol X-080, and Tween 80, and their effect on the extraction method. The tested values of the surfactant concentrations were 2, 5, and 10% *w*/*w*. Because low-surfactant concentrations in the one-step CPE resulted in less than 65% polyphenol recovery, requiring additional extraction methods, a three-step CPE method was implemented. The pH value and the sodium chloride concentration were also investigated. The optimum CPE conditions were established as a 30 min extraction at 55 °C, a pH value of 2.53, and a sodium chloride concentration at 3%. PEG 8000 was found to be the most effective of the four surfactants in most cases; notably, using only 2% of the surfactant per stage in a two-step CPE was adequate to effectively extract polyphenols with recovery rates greater than 99%. When 10% *w*/*v* PEG 8000 was employed, recoveries were more than 92%. Because PEG 8000 is a low-toxicity reagent, and the CPE method is simple, fast, cheap, sensitive, and selective, the chemical compounds extracted from apricot cannery waste can be employed as natural antioxidants in food technology. This has far-reaching consequences for the creation of natural and sustainable food additives. In a study published by Stramarkou et al. [83], the valorization of apricot pulp and kernels through the environmentally friendly method of ultrasound- and microwave-assisted extraction was investigated. Before the process, the pulps underwent a drying step, utilizing freeze, vacuum, and hot air-drying techniques. The findings of the research indicated that 80% ethanol proved to be the most efficient solvent for extracting apricot kernels. Additionally, a deep eutectic solvent containing choline chloride/urea diluted with water (7:3) exhibited higher efficacy in extracting apricot pulp, resulting in extraction yields of 25.65 and 26.83%, respectively. The findings indicate that, within an industry, the utilization of these techniques necessitates substantial expenditures on solvents and considerable energy consumption during the drying process when compared to the CPE method.

An overview of the application of cloud-point extraction on the bioactive components of food waste products is given by the studies mentioned above, which are all illustrated in Table 2.

Table 2. Overview of the implementation of cloud-point extraction on bioactive compounds of food waste products.

Matrix	Target Bioactive	Surfactant	Extraction Conditions	Extraction Yield (%)	Reference
Olive mill wastewater	Polyphenols	Tween 80 (10% *w*/*v*)	70 °C, pH 2, 30 min	75.5	[63]
	Polyphenols	Triton X-114 (2% *w*/*v*)	55–60 °C, 20 min	>90	[65]
	Polyphenols, tocopherols	Genapol X-080 (5% *w*/*v*)	55 °C, 20 min	-	[51]
	Natural antioxidants, polyphenols, carotenoids	Tween 80 (5–7% *w*/*v*)	55 °C, 30 min	-	[66]
	Polyphenols	Lecithin (3% *w*/*v*)	40 °C, pH 3.5, 20 min	42.2	[62]
	Polyphenols	Lecithin (12.5% *w*/*v*)	80 °C, pH 5.5	-	[67]
	Polyphenols	Triton X-100 (10% *w*/*v*)	90 °C, 30 min	66.5	[64]

Table 2. *Cont.*

Matrix	Target Bioactive	Surfactant	Extraction Conditions	Extraction Yield (%)	Reference
Olive leaves	Oleuropein, polyphenols	Tween 80 (4% *w*/*v*)	25 °C, pH 2.6, 5 min	93–100	[69]
Wine sludge	Polyphenols	PEG 8000 (2% *w*/*v*), Genapol X-080 (5% *w*/*v*)	55 °C, pH 2.5, 30 min	98.5 75.8	[71]
		Lecithin (5% *w*/*v*)	40 °C, pH 3, 30 min	76	[70]
Pomegranate peel	Polyphenols, flavonoids	Triton X-114 (8% *w*/*v*)	55 °C, pH 4.5, 30 min	94.48	[35]
	Polyphenols, flavonoids	Triton X-114 (10% *w*/*v*)	65 °C, pH 4, 40 min	-	[73]
Camu-camu residue	Polyphenols	Triton X-114 (7% *w*/*v*)	30 °C, 3 h	95.71	[75]
Mulberry leaves	Polyphenols Alkaloids	Triton X-114 (3% *w*/*v*) mixed with 0.05M HCl	25 °C, 45 min, ultrasonic power 360 W	89.2 85.9	[78]
Tomato liquid waste	Carotenoids	Lecithin (2% *w*/*v*)	45 °C, pH 3.5, 20 min	36.3	[80]
Apricot cannery waste	Polyphenols	PEG 8000 (2% *w*/*v*)	55 °C, pH 2.53, 30 min	>92	[82]

4. Discussion and Future Perspectives

Cloud-point extraction (CPE) is a highly advantageous method for extracting bioactive compounds from food biomass waste, since it combines rapidity, sensitivity, accuracy, and convenience. It is a green method, as it reduces the utilization of toxic solvents and does not require the use of organic solvents. Moreover, it requires no special equipment, so it is a cost-effective and easy-to-apply method. One of the key strengths of CPE is the utilization of mostly food-grade surfactants, making it safe for food applications. Moreover, emulsifiers, such as lecithin, can be utilized as surfactants. In addition, CPE can be combined with other methods, such as ultrasound-assisted CPE or microwave-assisted CPE, to further enhance the recovery of bioactive compounds. The utilization of CPE presents a favorable prospect for the simultaneous extraction of multiple bioactive compounds. Additionally, one notable advantage of CPE is the applicability of mild extraction conditions, thereby making it an ideal method for the extraction method.

Nevertheless, CPE has some limitations that need to be overcome in due time. Automating the sample-preparation step remains a challenge. Moreover, phase separation during the extraction of thermally labile components can be limited, especially when high temperatures are employed. While CPE is effective at a laboratory scale, scaling up the method to industrial levels can be complex. Factors such as the volume of waste material, extraction time, and cost-effectiveness need to be considered when implementing CPE on a larger scale. These limitations present opportunities for optimization and improvement in the future.

Nowadays, CPE is widely used to extract multiple bioactive compounds from food biomass waste. Existing methods can be further improved and applied to a wider range of food byproducts. Exploring and evaluating new surfactants and additives for CPE can enhance its effectiveness and selectivity. Investigating the use of other natural surfactants, such as saponins, alkylpolyglucosides, proteins, and peptides, or modified surfactants, can provide alternative options that are ecofriendly and compatible with food applications. Furthermore, exploring the extraction of other bioactive substances, such as proteins and enzymes, through CPE holds promise. Future research can focus on the simultaneous extraction of multiple bioactive compounds. Exploring the compatibility and interactions of different compounds in a single-extraction system can provide valuable insights into their coextraction behaviors and optimize the extraction of complex mixtures. Consequently,

the potential for expanding the applications of CPE in food-waste processing is vast and warrants further investigation.

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