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Aqueous biphasic systems as a key tool for food processing

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Aqueous biphasic systems (ABS) are widely known for their enhanced biocompatibility and selectivity in downstream processes. Hence, being a key tool for the extraction/separation of innumerous biomolecules. This is particularly important for the food industry considering the higher consumers' awareness for the health hazards associated with chemicals used in food processing and applications, as well as the replacement of synthetic food additives such as pigments and preservatives. Therefore, this mini-review offers a critical perspective on the progress done over the last three years regarding the application of ABS i) for the extraction of food-related biomolecules, ii) as analytical tools in food processing, iii) as *in situ* bio-based platforms, iv) for the valorization of food waste, and v) to shed some light on how molecular simulation approaches may be a key element in this framework.

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Introduction

World population is expected to reach nearly 10 billion by 2050 and with this a tackling pressure to intensify food production. Yet, food systems are increasingly vulnerable due to burdens on natural ecosystems and the climate [1]. Simultaneously, there is more awareness from the consumers to the hazards associated with the chemicals used, leading to higher demand for organic products, free of allergens and synthetic additives [2]. This is thus translated into a higher amount of food and/or biomass to be processed as well as a higher waste generation alongside the need for more sustainable and biocompatible strategies and solvents.

A key step in food processing and obtaining food by-products are the downstream processes (DSP) that not only allow the isolation and purification of food-related products but also allow the selective removal of contaminants. Among the different techniques applied for DSP, liquid–liquid extraction (LLE) represents a simple technology. This is especially the case of aqueous biphasic systems (ABS), which are a more biocompatible type of LLE [3,4]. ABS form two immiscible aqueous phases upon the combination of, at least, two water-soluble compounds, for example, polymers, salts, ionic liquids (ILs), alcohols, polysaccharides, and deep eutectic solvents (DES), above a critical concentration. This creates a mild environment suitable for a broad range of biomolecules such as proteins, antibiotics, and colorants, among others. Therefore, ABS have been widely proposed for DSP as they allow separation, concentration, and purification of compounds, usually in a single step, renowned as a simple and economic approach with easy scale-up [3–6].

This mini-review presents an overview of the most recent studies (≤3 years) regarding the use of ABS in food processing, namely i) in DSP, ii) as analytical tools, iii) as *in situ* bio-based platforms, and iv) for food waste valorization. Last, the advantages of using a modeling approach in food industry are also discussed. All studies performed during this period are summarized in Table 1 with a brief description of each study, the type of ABS, optimal conditions, and the best results obtained. In the meanwhile, the main innovations are also discussed in each section.

Aqueous biphasic systems as a tool for biomolecule extraction in food applications

Extraction, separation, concentration, and purification techniques are crucial steps in DSP, as these techniques are essential to isolate biomolecules from their complex sources in pure and active forms. At an industrial level, the established extraction techniques widely applied

include membrane separation, chromatography, ultrafiltration, precipitation, and solvent extraction using organic solvents, some with nonfavorable characteristics for biomolecules, the environment, and/or the operator. In addition, this means complex multiplestep operations with high-energy inputs and time-consuming methods. Besides, the sustainability of the entire operation, the manpower required and the operators' health and safety, the good manufacturing practices, recycling/reusing of chemicals, sterilization, and cleaning-in-place of equipment are also key components that must be taken into consideration when evaluating any biological and chemical process, especially considering today's *status quo* [3,6,84,85].

ABS have long been proposed to replace several of the previous operation units, mainly due to their 'integration ability', allowing to combine multiple steps in an integrated platform, not to even mention their greener, biocompatible, and more sustainable character [3,5,6,84]. Hence, there are innumerous studies with traditional and innovative ABS for the extraction and purification of food high added-value compounds with current high demand, namely specific proteins [20–30,41], enzymes [7–19], natural colorants [31–38], saponins [39,40], polysaccharides [42–45], and phenolic compounds [47–54,56,58]. Table 1 — Application A presents a brief description of all these studies as well as the best results achieved. Among these studies, it should be highlighted the use of aqueous two-phase flotation systems [20,21,51], a particular type of ABS, to improve the extractive performance, the application of sequential ABS for the fractionation and selective separation of multiple compounds present in the original samples [28,31], and the use of ABS in a continuous microextraction [56]. For an extensive analysis, in addition to the analysis of all details from Table 1, readers are also encouraged to check the recent reviews on these topics [2–4,6,84,86,87], and the Supporting information regarding to the biocompatibility and toxicity of the different phase formers.

Aqueous biphasic systems as an analytical tool

Overall, ABS are mainly used in two classical categories: i) DSP (previously discussed) and ii) samples pretreatment, mainly to concentrate the analytes. The latter is crucial for analytical quantification of different classes of samples, especially when the analytes are expressed in ppm, as is the case with the detection of various food elements.

Food safety is a major global health concern. Owing to irresponsible agriculture and industry practices, contaminants such as pesticides, veterinary residues, bacterial pathogens, heavy metals, environmental organic contaminants, and mycotoxins are present in our environment and are raising food safety concerns [88,89]. Since concentrations of these pollutants in sample matrices are low, pretreatment is required in order to enable accurate and sensitive determination of harmful compounds by eliminating unwanted interferences and enriching the target compound [5,82]. As ABS are able to concentrate samples up to 1000-fold (data for estrogen [90], a compound identified as a critical contaminant of food chains with several human health concerns [91]), they present themselves as a useful tool to improve analytical quantification.

In the past three years, the focus has been mainly on the detection of harmful compounds in food samples, such as dyes [60], cadmium [62], manganese [62], thiocyanate [83], mycotoxins [82], proteins [61], and pesticides such as fipronil [81], triazoles [63,64], and pyrethroids [64], as summarized in Table 1 — Application B. The detection of nutritional compounds, such as phenols, has also been reported [55]. ABS, for sample concentration, are replacing traditional techniques [63] and even novel procedures such as dispersive liquid–liquid microextraction [62]. The latter has also been reported to be used in tandem with ABS to promote the enrichment ability [82]. The importance of ABS in this field can be assessed in several recent reviews [92–95].

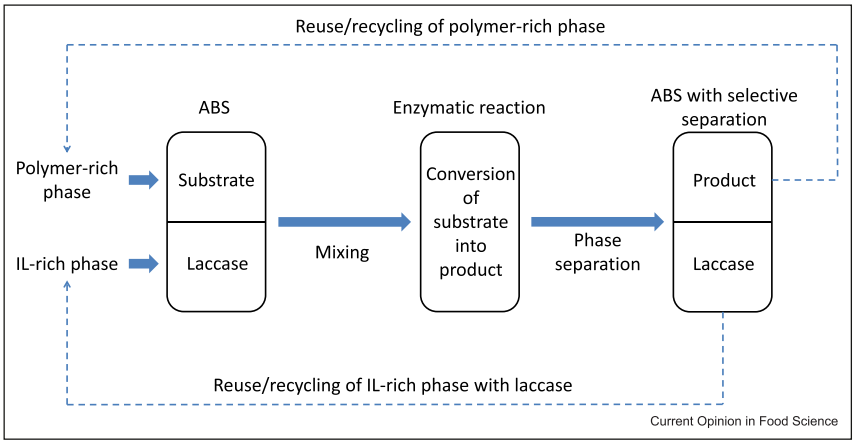
The curious part here is the fact that some of the ABS emerging in this topic are using water-miscible organic solvents (e.g. short alcohols, acetone, acetonitrile, and ethyl acetate) as one of the phase formers [71,81–83]. There has also been a case of an 'ABS' that consisted just of water and acetonitrile in 50–50 ratio, which puts it among classic LLE systems [81]. Regardless of the nature of the biphasic system, that is, organic–aqueous or aqueous–aqueous, these successful examples have demonstrated high usability and flexibility for food analytical purposes.

It is our belief that another important aspect regarding the use of ABS is related with the equilibrium of the ion (s) between the two phases. Among salt-based ABS, ion exchange between phases can raise some concerns, nonetheless, it has been proven a negligible phenomenon for ILs [96–100], whereas for DES-based ABS, the partition of the hydrogen bond acceptor and hydrogen bond donor is more commonly observed, leading to the formation of quaternary systems [101,102].

Aqueous biphasic systems as *in situ* bio-based platforms

Regardless of the multitude of combinations of phase formers, ABS have still been mainly studied as extraction/purification and concentration tools. Yet, these systems can still offer many interesting possibilities (further

Figure 1



Schematic representation of an ABS-based *in situ* biocatalytic platform for laccase. Adapted from Refs. [66,67].

discussed below), such as biocatalytic and fermentative *in situ* platforms, where ABS serve simultaneously as reaction/fermentation and purification medium, or as microcapsules for bioactive ingredient delivery.

Biocatalytic *in situ* platforms

Enzymes are fundamental in several fields, as they present excellent catalytic properties, selectivity, efficiency, low toxicity, and biodegradability. Laccases, for instance, are of special interest due to their capacity of oxidizing a wide range of molecules and thus, being able to catalyze several processes [65–67]. Without recycling, working with enzymes is expensive, so promoting their reuse with small compound losses or activity is crucial, albeit very challenging. Hence, ABS have been proposed as efficient liquid supports for laccase, allowing different *in situ* reactions (*cf.* Figure 1) [66,67]. Although these works are not directly related to food processing, they show outstanding results with the use and recycling of laccase in distinct reactions. Considering that laccase is an enzyme with food applications, we believe that these approaches can be extended to food processing. Herein, laccase and the products were recovered in distinct phases with enzyme extraction efficiencies (EE) > 90% and (relative) activity of 60–100%, whereas the product EE varied from 65% to 100%, even after 3–6 cycles. ABS components were also recovered and reused, promoting a sustainable approach.

Fermentative *in situ* platforms

Fermentations are frequently used in food industry to directly obtain different products, for instance, lactic acid bacteria fermentation in dairy industry, and yeast-based processes for bread, wine, and cider production. However, fermentation processes are susceptible to several limitations, namely sensitivities to (by-)product or substrate inhibition. This can be overcome through an ABS-based extractive fermentation or *in situ* product recovery, where one or two ABS' components are added to the cells and/or fermented broth for the formation of a biphasic system and, aiming the direct recovery of the product in the opposite phase to that where the microorganisms are growing and/or inhibitors are present [103]. Recently, this has been used to obtain food by-products such as preservatives [69,71] and colorants [70], where a backextraction can also be added to allow the phase former recovery and reuse in consecutive cycles [70].

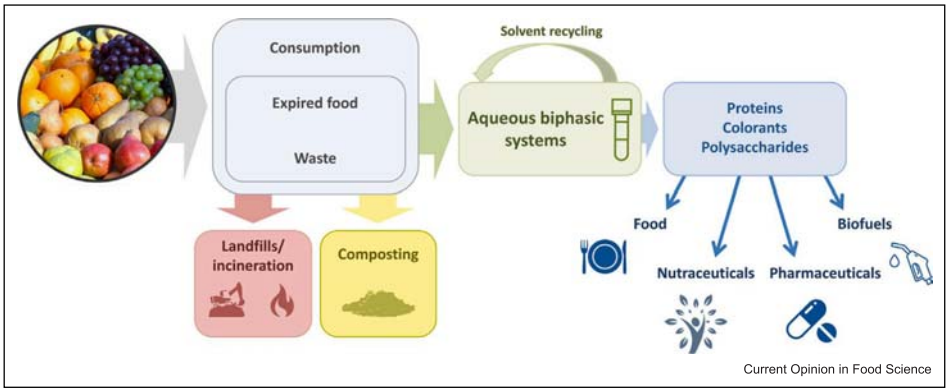
Delivery systems through microencapsulation

As for the innovative microencapsulation of bioactive compounds, Jiang et al. [68] proposed the formation of (collagen + pectin)–chitosan-based ABS microcapsules using the all-aqueous electrospray technique. They evaluated which combination of inner–outer phases would result in more stable microcapsules, that is, (collagen + pectin)–chitosan versus chitosan–(collagen + pectin), at different pH. When applied to anthocyanin encapsulation, these food-grade ABS microcapsules achieved ~93% efficiency, which is considerably higher than that obtained in aqueous core–shell–shell nanocapsules (34–55%) or with pectin–chitosan nanocarriers (67%). This is a good example representing an interesting development to replace conventional systems for loading and delivery of hydrophilic bioactive ingredients. ABS-based all-aqueous emulsions were recently reviewed in Ref. [104].

Valorization of food waste using aqueous biphasic systems

Around ⅓ of world food production (≈1.3 billion tons) is globally wasted every year, producing ≈ 4.4 gigatones of

Figure 2



Schematic representation of food waste valorization using ABS.

CO_2 equivalents, which is about 8% of world's total emissions [105]. Waste is being generated all the way from food production to retail and households. Therefore, considerable efforts should be dedicated to minimize this waste production. Waste valorization is not only an important tool for battling the growing environmental crisis, but also represents an opportunity for economic development. With the incorporation of the circular economy concept as an alternative of sending these residues to landfills or incineration plants, high added-value materials can be produced from discarded food compounds [106]. Thus, waste and excessive use of resources are minimized, while generating feedstocks for new products (Figure 2) [107]. It is clear that effective industrial implementation will only be achieved if greener, cheaper, simple, and more efficient systems are used for waste valorization. Further perspectives on this topic will be discussed in the last section.

Recently, ABS has been successfully applied for the extraction of several bioactive natural compounds (Table 1 — Application D) such as enzymes [78], proteins [80], and food additives [73]. These valuable molecules have previously been recovered from various sources that can be roughly split into expired food products [75,76] and by-products of agricultural industry [72–74,77–80] such as peels, seedcakes, fish residues, and so on.

Owing to the industry's continued reluctance to apply ABS as part of the production process and criticisms considering only simple lab-scale optimization of basic partition parameters (namely pH, temperature, and phase-forming components) [5], the research is slowly adding more factors that would make the technology more attractive for commercial use. These include the use of thermoseparating polymers that reduce recycling costs [72,78], pH-driven ABS that minimizes energy consumption [73], more advanced computing models [80], and implementation of continuous or semicontinuous operations [76].

Gao et al. [72] proposed a two-step ABS using a simple approach for polysaccharide extraction from seed cake. After a solid-liquid extraction (SLE) with DES, a thermosensitive polymer was added to form an ABS. The product then migrated toward the polymer-rich phase, which was separated from the DES-rich phase and heated to induce phase separation (2nd ABS formation) with product and polymer being recovered in opposite phases. This way, a more efficient separation was performed compared with the conventional system and simultaneously more economical than enzymatic extraction.

The waste valorizations were also shown by Yu et al. [73], where they performed fructose conversion using an ABS. The authors were able to replace crude fructose with apple peel and perform simultaneous extraction and conversion within the ABS [73,108].

Simulation approach as a tool to improve the aqueous biphasic systems-based applications in food industry

Multiscale simulation has been gaining prominence for the study of complex physicochemical phenomena. When applied to food industrial processes, it can be a useful decision-making tool concerning planning, designing, modeling, and preproduction evaluations [109–111]. Multicubed framework, for instance, assumes models at three scales: molecular microscale (describing thermodynamics), mesoscale of food structure (describing the evolution of dispersed phases), and macroscale of food products and processing equipment (describing transport phenomena between both) [112]. This multiscale modeling has been recently correlated

Table 1

Biomolecules being extracted and/or purified using different types of ABS for food purposes/applications, over the last three years. A brief description of each study, optimal conditions, and main results are also presented.

Compound	ABS	Description	Optimal conditions	Results	Ref.
Application A — ABS as a tool for biomolecule extraction in food applications					
Proteins and enzymes					
Proteases *Catalyze the hydrolysis of peptide bonds present in proteins and polypeptides. Used in brewing, milk coagulation, as flavor, digestibility and solubility enhancer, etc.*	**Polymer — salt** (PEG 1500 and 4000), (Na_3PO_4)	Partial purification of protease using ABS. Binodal curves and tie-lines were determined, and process parameters were optimized using statistical analysis.	PEG 1500 + Na_3PO_4, TLL = 35.955	Protease migrates preferably towards the most hydrophilic phase, that is, polymer-rich phase K = 0.451 K_e = 2.485 Activity yield ≈ 73% PF = 1.116	[7]
	Polymer — salt (PEG 400, 3350, and 8000), (Na_3Cit)	Protease was extracted using *Aspergillus tamarii* from different substrates. ABS was used for pre-purification of the product. Full factorial design 2^4 was applied to find the optimal PEG molecular weight, PEG and citrate concentrations and pH. Thermodynamics and kinetics were also studied.	20 wt% PEG 400 + 20 wt% Na_3Cit pH 8	Polymer-rich phase Activity yield ≈ 84% K = 4.6	[8]
	Polymer — salt (PEG 400, 3350, 8000), (PO_4^{2-})	Proteases produced by *Aspergillus tamarii* were extracted by ABS from the fermentation broth. Factorial design 2^4 was applied to find the optimum conditions (salt and PEG concentrations, PEG molecular weight and pH). The best conditions obtained on batch process were used on continuous extraction, where 2^2 factorial design was used to optimize disperse phase flow and continuous phase flow.	17.5 wt% PEG 8000 + 15 wt% of PO_4^{2} pH 6	Polymer-rich phase Batch Activity yield ≈ 113% PF = 2.62 Continuous Activity yield ≈ 147% PF = 1.84	[9]
	Polymer — salt (PEG 400, 3350, 8000), (Na_3Cit)	Proteases produced by *Aspergillus heteromorphus* were extracted with ABS. Factorial design 2^4 was applied in order to optimize PEG molar mass and concentration, citrate concentration and pH. Biochemical, kinetic and thermodynamic parameters were later evaluated.	24 wt% PEG 8000 + 15 wt% Na_3Cit pH 8	Polymer-rich phase K = 7.83 Yield ≈ 158%	[10]
	Polymer — salt (PEG 1500, 4000 8000), (Na_3PO_4)	Partial purification of fibrinolytic and fibrinogenolytic protease was performed by ABS. Factorial design was used to find optimal conditions. Effects of metal ions, temperature and pH and were evaluated.	12.5 wt% PEG 8000 + 15 wt% Na_3PO_4 pH 8	Polymer-rich phase PF = 6.26 K = 1.32 Yield ≈ 142%	[11]
Microbial transglutaminase *Catalyzes the formation of isopeptide bonds between proteins. Used in cheese and other dairy products*	**Copolymer — copolymer** (P_{NE}), ($P_{ADB4.91}$, P_{NDBN})	Thermosensitive and thermo-pH sensitive ABS were applied for partition of microbial transglutaminase. After designing thermos-sensitive polymer, ABS were formed and binodal curves	2.5% (w/v) P_{NE} + 3.5% (w/v) $P_{ADB4.91}$ + 10 mM KCl 25°C, pH 7, and 2 mg/mL of substrate	Polymer-rich phase Rec. ≈ 95% K = 12.9	[12]

Table 1 (*continued*)

Compound	ABS	Description	Optimal conditions	Results	Ref.
manufacturing, bakery manufacturing, edible film production in meat processing etc.		designed. Parameters (substrate amount, pH and temperature) of partition were studied. Salt addition was explored.			
Ovalbumin and lysozyme *Ovalbumin is used as a nutrient supplement and as an allergen to establish models food allergies. Lysozyme is used as a food preservative.*	**IL — salt** (tetraalkylammonium-based) (K_2HPO_4/KH_2PO_4 or K_3PO_4)	Several different tetraalkylammonium IL — phosphate-based ABS were evaluated as media for extraction of ovalbumin and lysosome at different pH values. Binodal curves were designed for all systems at different pH and EE were studied. Interactions on molecular level were investigated.	21–35 wt% $[N_{2,2,2,2}]Br$/$[N_{2,2,2,2}]Cl$ + 16–24 wt% K_2HPO_4/KH_2PO_4 pH 7 for ovalbumin (shorter chains and lower hydrophobicity produce better results), for lysozyme all worked well between pH 7 and 9 in the same composition region	IL-rich phase EE = 100% Rec. = 100%	[13]
Prolyl endopeptidase *Used to debitter protein hydrolyzates, prevent chill-haze in beer and eliminate gluten by degradation of proline-rich proteins, and alleviate celiac disease symptoms.*	**Alcohol — salt** (EtOH), ($(NH_4)_2SO_4$)	Separation of prolyl endopeptidase produced by *Aspergillus niger* from fermentation broth. Response surface methodology was applied to optimize pH, and ABS components concentrations. Effect of temperature, pH, and metal ions on enzyme activity was evaluated, followed by enzyme kinetics. Enzyme was then used for hydrolysis of egg protein in order to prepare bioactive peptides.	4.5 wt% $(NH_4)_2SO_4$ + 27 wt% EtOH pH 6	Salt-rich phase PF = 15.35 Rec. ≈ 90%	[14]
Lipase *Used as a flavor enhancers.*	**Polymer — salt** **Alcohol — salt** (PEG 4000), (2-propanol), ($(NH_4)_2SO_4$)	Lipase extracted from pequi seed was partitioned in ABS. The objective was to evaluate the influence of temperature. Binodal curves were designed for both systems and partition was tested at two different temperatures for crude extract and precipitate.	20 wt% 2-propanol + 17.5 wt % $(NH_4)_2SO_4$ 25°C	Yield ≈ 86% PF = 4.48 K = 0.931 K_e = 0.053	[15]
Amylase *Hydrolyzes polysaccharides. Used in baking, brewing, starch liquefaction and as a digestive aid.*	**Polymer — salt** (PEG 4000, 6000) (Li_2SO_4, $(NH_4)_2SO_4$, Na_2SO_4)	Solid state fermentation of *Aspergillus niger* to produce amylase. Binodal curves were designed. Enzyme precipitation with $(NH_4)_2SO_4$, which was used for its isolation from total proteins using ABS. Thermodynamic modeling was performed using the UNIFAC model.	15 wt% PEG 4000 + 11 wt% $(NH_4)_2SO_4$ + 74 wt% H_2O	Polymer-rich phase Theoretical recovery$_{amylase}$ ≈ 80% $K_{amylase}$ = 3.42 $K_{total\ proteins}$ = 1.69	[16]
β-fructofuranosidase *Used for the synthesis of fructo-oligosaccharides that have a prebiotic role, as well as ingredients in functional foods, such as baking and dairy products, breakfast cereals, frozen desserts, infant formulae, fruit preparations, dietetic*	**Polymer — salt** (PEG 400, 3350, 8000), (Na_3Cit)	β-fructofuranosidase from *Aspergillus tamarii* was purified with the use of ABS. Factorial design was applied to optimize purification parameters. Effects of pH, temperature, metal ions and ultrasound on activity of the enzyme were evaluated. At the end, kinetics was investigated.	24 wt% PEG 400 + 20 wt% Na_3Cit pH 8	Salt-rich phase PF = 6.42 Yield ≈ 350%	[17]

Table 1 (*continued*)

Compound	ABS	Description	Optimal conditions	Results	Ref.
products, and sweeteners.					
Pepsin *Hydrolyzes proteins into smaller peptides. Used to prepare proteins for flavoring use, to provide whipping qualities to gelatin and soy protein and in cheese parathionion.*	**Polymer — DES** **Polymer — DES component** (Betaine HCl (BeHCl)) (PPG 425), (BeHCl + fructose, glucose, sucrose, and urea)	Simultaneous extraction and recovery of pepsin. Binodal curves were designed. Cytotoxicity and biocompatibility were tested. EE and activity were measured at fixed conditions.	35 wt% PPG 425 + 20 wt% BeHCl-glucose DES + 45 wt% water	More hydrophilic phase — DES (component)-rich phase Rec. = 142% EE ≈ 100%	[18]
Tannase-acyl hydrolase *Catalyzes the hydrolysis of tannins to gallic acid and glucose. Used to reduce the bitter taste of tannin, which improves the flavor of the products, such as green tea.*	**Polymer — salt** (PEG 1000, 3350, 6000), (Na_3Cit)	Extraction of tannase-acyl hydrolase obtained from *Aspergillus sydowii* using ABS. With the use of statistical design extraction process was optimized and temperature, pH, metal ions and surfactant effect were studied. Enzyme was later used for detannification of green tea.	24 wt% PEG 6000 + 20 wt% Na_3Cit	Salt-rich phase PF = 3.2 Activity yield ≈ 94% K = 0.1	[19]
α-lactalbumin k *Main component of whey, a protein by-product in milk production, with a good nutritional value and different good functional properties.*	**Polymer — salt** (poly (ethylene glycol-ran-propylene glycol) monobutyl ether (UCON)), (KH_2PO_4)	Separation and purification of α-lactalbumin from cow milk whey using aqueous two-phase flotation, consisting of thermos-sensitive polymer and salt. The article investigated effects of system composition and operating parameters on flotation efficiency and purity. Recovery of the polymer was also investigated.	4.8 wt% UCON + 15 wt% PO_4^{3-} + 4.8 wt% NaCl 2 min of premixing time, 30 mL min^{-1} flow velocity, 20 min of flotation time	Polymer-rich phase Flotation efficiency ≈ 96% Purity ≈ 99%	[20]
α-lactalbumin *Great source of essential amino acids as the second most abundant protein in bovine whey.*	**Polymer — salt** (PEG 1000), (Na_3Cit)	Aqueous two-phase flotation system was applied, and process conditions were optimized. Binodal curves were designed, and single-factor experiments were coupled with factorial design.	6.3 wt% 14 PEG 1000 + 35% Na_3Cit pH 8.2, 30 mL min^{-1} of flow velocity, 42 min of flotation time	Polymer-rich phase PF ≈ 5.3 EE ≈ 88%	[21]
Proteins *Great source of essential amino acids. Used a food supplement and/or in sweets, pastas and beverages.*	**Polymer — salt** (PEG 1500, 4000, 6000, and 8000), (K_3PO_4, Na_3Cit)	Purification of proteins from *Arthrospira platensis* was optimized using factorial design, independent variables being salt and polymer concentrations.	16 wt% Na_3Cit + 18 wt% PEG 1500 pH 9	Polymer-rich phase Rec. ≈ 75% PF = 1.02	[22]
BSA *Major bovine plasma protein that binds and carries biological molecules. Used as a food ingredient.*	**Polymer — salt** (PEG 4000), (Na_3Cit)	ABS was tested in a microfluidic device for separation of BSA. Microchannel length, flow rate, and pH, were investigated using factorial design.	19.7 wt% PEG 4000 + 20.4 wt % Na_3Cit Microchannel length: 8 cm, salt flow rate: 1.87 mL h^{-1}, pH 6.92	Polymer-rich phase Rec. ≈ 71%	[23]
	IL — salt (several different ILs, *cf.* [24] for more details) (K_2HPO_4/KH_2PO_4)	Herein extraction of BSA was performed from bovine serum. Imidazolium-, phosphonium-, and ammonium-based ILs were used in a combination with phosphate buffer to assemble ABS. Binodal curves were designed, then partition of pure BSA was tested and later bovine serum	35 wt% $[N_{4,4,4,4}][Ac]$ + 20 wt% K_2HPO_4/KH_2PO_4 pH 7 + 45 wt % (1:15; v-v) bovine serum aqueous solution	IL-rich phase Rec. ≈ 86%	[24]

Table 1 (*continued*)

Compound	ABS	Description	Optimal conditions	Results	Ref.
		was used for the most optimal system.			
BSA, IgG and Cyt C *IgG is the major antibody group in mammals.* *Used as an important indicator of food allergies.* *Cyt C is a hemeprotein important for function of mitochondria and is stimulated by food-derived polyphenols.*	**Polymer — polymer** (PEG 400, 6000, and dextran 450–650)	Binodal curves were designed for quaternary ABS with ILs as adjuvants (5 and 10 wt%). Screening of imidazolium-, pyridinium-, pyrrolidinium-, piperidinium-, tetraalkylphosphonium-, and tetraalkylammonium-based ILs with the same alkyl side chain (C = 4) and anion (Cl^-). Partitioning studies using three proteins. Best systems were compared with quaternary polymer–salt ABS. Molecular interactions were studied through molecular docking.	5 wt% PEG 6000 + 10 wt% dextran 450–650 + 5 wt% $[P_{4,4,4,4}]Cl$.	ILs as adjuvants tailor the proteins partitioning. BSA and IgG migrated preferably to the dextran-rich phase. Cyt C partitioned preferably to the PEG-rich phase.	[25]
BSA, lactalbumin and lactoglobulin *Lactalbumin and lactoglobulin are whey proteins found in milk.* *Used as food supplements.*	**Polymer — salt** (PEG 200, 300, 600, 1500, 4000, 8000), (Na_2SO_4, $(NH_4)_2SO_4$)	Separation of whey proteins from lactose was studied. Binodal curves were designed. BSA, α — lactalbumin, β — lactoglobulin and lactose partition was studied in systems with different molecular weight PEG and two different salts, namely Na_2SO_4 and $(NH_4)_2SO_4$. Then, pH was optimized.	PEG 1500 — $(NH_4)_2SO_4$ is able to separate lactose from proteins, while PEG 300 — Na_2SO_4 ABS can be used for protein fractionation	Protein precipitate Rec. > 95% Salt-rich phase Lactose Rec. > 80%	[26]
R-phycoerythrin *Bioactive protein found in algae.* *Used in food industry as a natural pigment.*	**DES — salt** ([Ch]Cl-based), (K_2HPO_4)	Protein R-phycoerythrin from marine algae was purified using DES-based ABS. Binodal curves were designed for multiple systems and their extraction ability was screened. Single factor experiments were performed for the best one.	0.35 g [Ch]Cl — urea + 0.8 g/mL, 0.5 mL K_2HPO_4 0.04 mg protein load 20–30 min extraction time	EE ≈ 93% Yield ≈ 70%	[27]
Cyanobacterial phycobiliproteins (phycocyanin and allophycocyanin) *Pigment-protein complexes.* *Used as protein source and natural food colorants in ice creams, soft drinks and sweets.*	**Polymer — salt** (PEG 6000), (K_2HPO_4/KH_2PO_4)	Two-step ABS was used in a tandem with ultrafiltration for purification of cyanobacterial phycobiliproteins. Effect of surfactant treatment on preparation of crude lysate was evaluated. First step was purification of phycobilisome in ABS which was followed by phycobiliprotein purification performed by the second ABS. Four different cyanobacteria were tested.	1st step: 10 wt% PEG 6000 + 14.5 wt% K_2HPO_4/KH_2PO_4 buffer system 2nd step: 10 wt% PEG 6000 + 16.1 wt% K_2HPO_4/KH_2PO_4 buffer system	1st step: Phycobilisome Rec. ≈ 97% Polymer-rich phase Phycocyanin Rec. ≈ 97% Salt-rich phase Allophycocyanin Rec. ≈ 95%	[28]
	Polymer — salt (PEG 1500), (K_3PO_4, Na_3Cit, $(NH_4)_2SO_4$)	Phycobiliproteins were extracted from *Anabaena variabilis* and *Nostoc* sp. strains. Different ABS based on PEG 1500 and different salts were studied.	***Anabaena variabilis*** 13 wt% PEG 1500 + 14 wt% K_3PO_4 ***Nostoc* sp.** 13 wt% PEG 1500 + 14 wt% Na_3Cit	Polymer-rich phase *Anabaena variabilis* $K_{PC} = 8.63$ $K_{APC} = 5.11$ $K_{PE} = 4.94$ *Nostoc* sp. $K_{PC} = 17.18$ $K_{APC} = 32.65$ $K_{PE} = 7.15$	[29]
	Polymer — salt (PEG 1500, 4000) (K_3PO_4 and Na_3Cit)	After extraction of phycocyanin, done by freezing method and ultrasonic bath,	10 wt% PEG 1500 + 15.9 wt% K_3PO_4 pH 7.17	Polymer-rich phase *Anabaena variabilis* Rec. ≈ 82% K = 5.74	[30]

Table 1 (*continued*)

Compound	ABS	Description	Optimal conditions	Results	Ref.
		different ABS were used for recovery of the product.		*Nostoc* Rec. ≈ 79% K = 6.36	
Natural colorants					
Betalains *Found in pitaya and other fruit. Used as pigments that produce several tonalities, from yellow-orange to red-purple.*	**Alcohol — salt** (1-propanol), (Na_3Cit)	Betalains from pitaya fruit were separated from phenols and sugars and further partitioned into Bc and Bx betalains. Binodal curves were constructed. For this purpose, multistage ABS was designed.	2nd step: 6.6% Na_3Cit and 60.5% 1-propanol	1st step Salt-rich phase total soluble phenols sugars Bc betalains Bx betalains 2nd step Alcohol-rich phase EE > 90% Bx betalains alcohol Rec. ≈ 46% Salt-rich phase Bc betalains Rec. ≈ 54% (of the initial Bx and Bc betalains)	[31]
Astaxanthin *Has antioxidant activity.* *Used as a natural colorant due to its color and high stability.*	**Alcohol — salt** (1-propanol, 2-propanol, EtOH) (Na_3Cit, KH_2PO_4/ K_2HPO_4, $(NH_4)_2SO_4$))	Astaxanthin was extracted from *Kluyveromyces marxianus.* Effect of ultrasonication time, alcohol and salt type combinations, phase composition, yeast cell loading, pH and adjuvants were studied in each step. At the end, ABS with and without ultrasonication were compared.	20 wt% 1-propanol + 20 wt% Na_3Cit + 0.5 wt% yeast cells loading and addition of 1 wt% $[C_4mim]BF_4$ pH 5, 2 hours ultrasound	Alcohol-rich phase K = 90 Yield ≈ 97% EE ≈ 86%	[32]
	IL — salt (phosphonium- and ammonium-based IL), (K_3PO_4)	Shrimp waste was used for extraction of astaxanthin by ABS. Phosphonium- and ammonium-based ILs were combined with K_3PO_4. Binodal curve was designed and properties (density, viscosity, and pH) of systems were evaluated, thermodynamic measurements were made and reusability of IL was studied.	25 wt% $[P_{4,4,4,8}]Br$ + 15 wt% K_3PO_4 + 60 wt% of H_2O. SLR = 1:20 g/mL, 35°C, 12 hours	IL-rich phase EE ≈ 93%	[33]
Lycopene *Antioxidant responsible for red color of fruits and vegetables.* *Used as a colorant and as a food supplement.*	**Polymer — salt** (polyvinylpyrrolidone 10 000) (Na_2SO_4, $ZnSO_4$, $Na_2C_4H_4O_6$)	Lycopene partition was evaluated in several ABS composed of polyvinylpyrrolidone 10 000 and different salts. Binodal curves were designed and effects of different parameters, namely temperature and pH, were evaluated.	polyvinylpyrrolidone 10 000 + Na_2SO_4 pH and temperature have negligible effect	Polymer-rich phase K = 23.6	[34]
Anthocyanins *Pigments responsible for the dark purple color of fruits.* *Used as a natural colorant.*	**Alcohol — salt** (EtOH), ($(NH_4)_2SO_4$)	Microwave assisted extraction and purification was performed using anthocyanins from *Rosa pimpinellifolia* L. Single factor experiments and response surface methodology were applied. HCl additions were studied; however 0% HCl proved to be the most efficient. EtOH and	26.9 wt% EtOH + 19.2 wt% $(NH_4)_2SO_4$, SLR = 0.025, 17 min, 60°C and 400 W	Alcohol-rich phase Yield = 1370 mg/100 mg dry biomass	[35]

Table 1 (*continued*)

Compound	ABS	Description	Optimal conditions	Results	Ref.
		$(NH_4)_2SO_4$ concentrations and extraction time were the significant parameters determined from single-factor experiments and optimized with response surface methodology.			
Curcumin *Polyphenol found in turmeric.* *Used as spice, a dietary supplement and as a colorant.*	**Polymer — salt** **Copolymer — salt** (PEG 2000, 6000, PPG 400, Pluronic L3), (Na_2SO_4, $MgSO_4$)	System for separation of curcumin was developed based on polymer–salt ABS. Binodal curves were designed for different compositions of ABS. Different systems were tested, effect of temperature was evaluated, and polymer-curcumin interactions were studied.	19–40 wt% Pluronic L35 + 9–13 wt% Na_2SO_4 25°C	Polymeric micelles-rich phase K > 200	[36]
	Copolymer — buffer (Pluronic F68), (McIlvaine buffer)	In order to separate and purify curcumin, ABS composed of copolymer and McIlvaine buffer was studied. ILs were used as adjuvants. After binodal curves were designed for systems with different ILs, stability studies were made. Two systems with the best partition were selected to study further.	1 wt% Pluronic F68 + McIlvaine buffer + 0.60 M [Ch][Hex] 25°C, pH 6	Polymeric micelles-rich phase Rec. ≈ 92% K = 25 PF = 15	[37]
	Polymer — salt (Poly(vinylpyrrolidone) 10 000), (Li_3Cit)	For the partitioning of curcumin, polymer–salt ABS was applied. Binodal curves were designed, and partition of curcumin was studied at different temperatures using mathematic modeling.	15.1 wt% poly (vinylpyrrolidone) 10 000 + 19.6 wt% Li_3Cit 25°C	EE ≈ 90% K = 21.2	[38]
Saponins					
Saponins *Naturally occurring compounds.* *Used as a food supplement.*	**IL — base** ($[C_4mim]BF_4$), (NaOH)	Saponins extracted from *Momordica charantia* L. using high hydrostatic pressure were purified with ABS. Process was optimized using factorial design (with IL and NaOH concentrations, SLR as independent variables).	2.15 M $[C_4mim]BF_4$ aqueous solution + 9.9 wt% NaOH SLR = 1:10.5	Base-rich phase Purity ≈ 76%	[39]
	Polymer — polymer (poly-(N-isopropylacrylamide (P_N), poly-(acrylic acid-dimethylamine ethyl methacrylate-butyl methacrylate ($P_{ADB4.78}$))	Tea saponins were partitioned in thermo-pH sensitive ABS. Binodal curves were designed. Temperature, pH, polymer concentrations and salt (KCl and LiBr) additions effects were tested. After saponin partition, both polymers were recycled (recoveries >93%) using temperature and pH changes.	1.5% (w/v) P_N + 3.5% (w/v) $P_{ADB4.78}$ + 7.5 mM LiBr pH 8 and 25°C	$P_{ADB4.78}$-rich phase K = 0.12 Rec. ≈ 95%	[40]
Ginsenoside *Active ingredient of ginseg.* *Used as a dietary supplement.*	**DES — salt** (ChCl + urea, ethylene glycol/glucose/glycerol), (K_2HPO_4)	Extraction and transformation of ginsenoside from ginseng using β-glucosidase within the ABS. Activity and half-life of the enzyme in different DESs were studied. Binodal curves were designed. Single-factor experiments were performed for optimization of the process parameters and recycling of	31.9 wt% [Ch]Cl–ethylene glycol + 24.5 wt% K_2HPO_4 55°C, pH 5	DES-rich phase Ginsenoside Rec. ≈ 76% K = 4.77 Salt-rich phase β-glucosidase Rec. ≈ 61% K = 0.71	[41]

Table 1 (*continued*)

Compound	ABS	Description	Optimal conditions	Results	Ref.
		DES and β-glucosidase was evaluated.			
Polysaccharides					
Solanine and polysaccharides *Solanine is a glycoalcaloid found in different kind of plants and with many health-beneficial characteristics. Polysaccharides have immune and antimicrobial functions for humans, besides being nutritious.*	**Alcohol — salt** (EtOH), (KOH, $(NH_4)_2SO_4$, NaH_2PO_4, K_2CO_3, K_2HPO_4, Na_2SO_4, K_3PO_4)	Polysaccharides and solanine (solasonine and solamargine) were extracted from *Solanum nigrum* fruit. Cell walls were disrupted with ultrasonication. Partition efficiencies were measured in several ABS (different salts). Factorial design was performed with three independent variables: temperature, EtOH and salt concentration in order to achieve the highest partition coefficient.	36 wt% EtOH + 21% (w/v) K_2CO_3 15°C	Alcohol-rich phase Solasonine partition efficiency ≈ 96% EE ≈ 2.2 mg g^{-1} Solamargine partition efficiency ≈ 97% EE ≈ 2.3 mg g^{-1} Salt-rich phase Solanum nigrum polysaccharide partition efficiency ≈ 97%. EE = 9.1 mg g^{-1}	[42]
Polysaccharides	**IL — salt** ($[C_4mim]Cl$, $[C_6mim]Cl$, $[C_8mim]Cl$, $[C_{10}mim]Cl$), (K_2CO_3)	Extraction and purification of sorghum leaf sheath polysaccharides. Phase diagrams were designed. EtOH–water mixture in different compositions was used to form ABS, which was combined with ultrasound. Box-Behnken Design was applied (variables being time, dual frequency of ultrasound and temperature). Antioxidant activity was also studied.	35 wt% $[C_8mim]Cl$ + 17 wt% K_2CO_3 + 48 wt% EtOH:water (40:60 wt%) 35°C, 20–60 kHz dual frequency, and 30 min	Salt-rich phase Yield = 16%	[43]
	Alcohol — salt (EtOH), (K_2HPO_4, $(NH_4)_2SO_4$, NaH_2PO_4)	*Lycium barbarum* L. fruits polysaccharides were extracted. Binodal curves were designed for all EtOH-based systems. Then single-factor experiments (time, tissue-smashing power, SLR, salt and EtOH concentrations) were followed by factorial design. Comparison with conventional methods was made.	28.9 wt% EtOH + 17.9 wt% $(NH_4)_2SO_4$ SLR 0.03, tissue-smashing power 8000 rpm, extraction time 4 min	Salt-rich phase Yield ≈ 25 mg g^{-1}	[44]
Exopolysaccharides *Used as thickeners, emulsifiers or stabilizers.*	**Polymer — salt** (PEG 600), (NaH_2PO_4)	Exopolysaccharides from *Lactobacillus plantarum* separation by ABS. Single-factor design combined with the response surface method. At the end, antioxidant and hypoglycemic activity and inhibitory kinetics were studied.	22.5 wt% PEG 600 + 17 wt% NaH_2PO_4 pH 6	Salt-rich phase K = 5.25 Yield ≈ 72%	[45]
Preservatives					
Parabens *Used as preservatives and antimicrobial agents.*	**Polymer — salt** (PEG 400, 2000, 6000 and PPG 400), ($(NH_4)_2SO_4$)	Parabens were removed and concentrated using ABS. Binodal curves were prepared. Effect of TLL was evaluated for different combinations of polymers and salt.	11.5 wt% PPG 400 + 11 wt% $(NH_4)_2SO_4$	Polymer-rich phase EE ≈ 100% K > 300	[46]
Phenolic compounds					
Caffeine, codeine, vanillin, and curcumin *Vanillin is a well-used flavoring agent.*	**Polysaccharide — polymer** **Polysaccharide — alcohol** (sucrose, glucose), (PPG 400), (1-propanol)	Caffeine, codeine, vanillin, and curcumin were extracted using polysaccharide-based ABS. Binodal curves were designed. Partition patterns of	28 wt% sucrose + 30 wt% PPG 400	Polymer-rich phase Caffeine K = 2.05 Vanillin K = 19.75 Curcumin	[47]

Table 1 (*continued*)

Compound	ABS	Description	Optimal conditions	Results	Ref.
Caffeine is an alkaloid used in food industry as a stimulating drug for the brain and nervous system. Codeine is an opiate and prodrug of morphine and is mainly used to treat pain and diarrhea. Curcumin is a polyphenol used as a spice and a colorant.		four molecules were thoroughly studied.		K = 246.37 Sugar-rich phase Codeine K = 0.059	
Caffeine, lamotrigine, clonazepam and oxcarbazepine *Lamotrigine is a pharmaceutical drug used to treat epilepsy and bipolar disorder. Clonazepam is a medication used to treat seizures and a variety of mood disorders. Oxcarbazepine is a medication used to treat epilepsy.*	**Polymer — DES** **Polymer — IL** (polyethylene glycol dimethyl ether 250 ($PEGDME_{250}$)), ([Ch]Cl-saccharose), ([Ch]Cl)	Several different biomolecules were partitioned in polymer-DES ABS. Binodal curves were designed for systems with different compositions of DES and different temperatures. Later, partition behavior was studied.	58.3 wt% $PEGDME_{250}$ + 26.2 wt% [Ch]Cl 25°C	Polymer-rich phase Caffeine K = 6.26 EE ≈ 86% Oxcarbazepine K = 20.50 EE ≈ 95% Lamotrigine K = 43.08 EE ≈ 98% Clonazepam K = 65.71 EE ≈ 99%	[48]
Chlorogenic acid, flavonoids, total phenolic compounds (TPC) *Chlorogenic acid is a phenolic compound found in many foods with antioxidant properties. Total phenolic compounds are important plant antioxidants which are used as biopreservatives. Flavonoids are found in a wide variety of foods and are used as dietary supplements, colorants and preservatives.*	**Alcohol — salt** **Sugar — alcohol** (EtOH, 1-propanol), (maltose, glucose), ($(NH_4)_2SO_4$, NaH_2PO_4)	With the use of salt–EtOH and sugar–propanol ABS, bioactive compounds were extracted from *Lonicera caerulea* leaves. Binodal curves were designed. Response surface regression model was applied, where tie-line length, sample loading and extraction time were picked as variable parameters.	37 wt% EtOH + 10 wt% NaH_2PO_4, 53 wt% water	Alcohol-rich phase Chlorogenic acid EE ≈ 94% K = 1.73 Flavonoids EE ≈ 97% K = 3.5 Total phenols EE ≈ 98% K = 6.59	[49]
	Alcohol — salt **Polysaccharide — alcohol** (EtOH, 1-propanol), ($(NH_4)_2SO_4$, NaH_2PO_4), (glucose, maltose)	This research evaluated the effects of recycling several ABS components on the extraction of several bioactive compounds. Optimal process parameters were taken from their previous study [49].	37 wt% EtOH + 10 wt% NaH_2PO_4	Alcohol-rich phase EE all above 99.5% TPC K = 28.85 Yield ≈ 0.08 mg GAE mg^{-1} Flavonoids K = 28.17 Yield ≈ 0.25 mg RE mg^{-1} CGA K = 10.99 Yield ≈ 41 μg CGA mg^{-1}	[50]
	Alcohol — salt (EtOH), ($(NH_4)_2SO_4$, Na_3PO_4)	Aqueous biphasic flotation was used for extraction of bioactive compounds from haskap leaves. Box-Behnken design and response surface approach were used for optimization. Optimized system was later compared with ABS, conventional method, and water with and without flotation extraction.	20 wt% $(NH_4)_2SO_4$ + 27.5 wt% EtOH + 52.5 wt% water 120-min flotation time, and air flow rate of 28.6 mL min^{-1}	Alcohol-rich phase Chlorogenic acid EE ≈ 97% K = 29.6 Flavonoids EE ≈ 99% K = 62.4 Total phenolic content EE ≈ 100% K = 231.4	[51]

Table 1 (*continued*)

Compound	ABS	Description	Optimal conditions	Results	Ref.
Rutin and quercetin Two flavonoids that are being used as supplements due to their roles as cell-protecting agents.	**Organic solvent — salt** (ethyl lactate), (K_3Cit, Na_3Cit)	Purification of rutin and quercetin was studied. Binodal curves were designed and thermodynamic studies were performed. Influence of salt cation on partition was evaluated.	12.6 wt% ethyl lactate + 40.6 wt% Na_3Cit	Rutin K = 12.72 EE ≈ 95% Quercetin K = 25.91 EE ≈ 97%	[52]
Phenolic compounds *Natural bioactive molecules with antimicrobial properties. Used as preservatives.*	**Alcohol — salt** (EtOH), ($(NH_4)_2SO_4$)	ABS combined with microwaves was used for extraction of phenolic compounds from *Ribes nigrum* L. Binodal curve was prepared, and ABS was compared with solvent, ultrasound assisted, and microwave assisted extractions. After extraction product was purified using macroporus resin. Antibacterial activity analysis was later made.	28.3 wt% EtOH + 14.3 wt% $(NH_4)_2SO_4$ SLR 0.014, 65°C, 10 min, and 600 W microwave power	Alcohol-rich phase Yield ≈ 59 mg g^{-1} Rec. ≈ 81%	[53]
	Polymer — salt **Organic solvent — salt** (PEG 2000), (acetone), (Na_3Cit)	Phenolic compounds were separated from *Hibiscus sabdariffa*. Binodal curves were designed, and factorial designed was performed. Sugar separation from the product was also evaluated using sucrose as a model compound.	15.8% PEG 2000 + 25.2% Na_3Cit	Polymer-rich phase Phenolic compounds Rec. ≈ 95% K = 19.23 Yield ≈ 90% Salt-rich phase Sugars Rec. ≈ 93% K = 0.41 Yield ≈ 78%	[54]
	Alcohol — salt (iso-propanol, n-propanol, EtOH), (Na_3Cit), ($(NH_4)_2SO_4$)	ABS was developed and coupled with multivariate chemometric methods to detect phenolic compounds in tea samples. Different ABS were used for extraction. And the most promising sample was used for further analysis.	35.6 wt% iso-propanol + 0.7 wt% Na_3Cit + 11.6 wt% $(NH_4)_2SO_4$ + 52.1 wt%	Alcohol-rich phase Rec. ≈ 83–111% LOD — 1.3–305.9 mg L^{-1} LOQ — 3.9–927 mg L^{-1}	[55]
Polyphenolic compounds *Organic compounds that are abundant in plants and present antioxidant and anti-inflammatory properties.*	**DES — salt** ([Ch]Cl + citric acid/ethylene glycol/glycerol/glucose), (K_2HPO_4)	Continuous microextraction process of polyphenolic compounds was developed. After screening of different ABS (changing the DES component), [Ch]Cl–ethylene glycol DES was picked as a most promising one for further analysis. The effects of DES mass, extraction time, extraction temperature, salt concentration and gallic acid concentration on the batch EE have been investigated using Box-Behnken design and mathematic modeling. Then continuous micro-extractor was used under these conditions and 2D model was developed considering flow direction and diffusion.	1.25 g [Ch]Cl–ethylene glycol + 2 mL 0.95 g/mL K_2HPO_4 15 min, 50°C Batch: t = 15 min Continuous: τ = 3.65 s	DES-rich phase Batch: EE ≈ 88% Continuous: EE ≈ 94%	[56]
Gallic acid *Hydrophilic polyphenol present in plants with*	**Alcohol — salt** (1-Propanol, 2-Propanol, EtOH) (Na_3Cit, K_2HPO_4/KH_2PO_4, $(NH_4)_2SO_4$)	Partition of gallic acid was studied. Different ABS were constructed based on curves from their previous study [57].	24 wt% 1-propanol + 22 wt% phosphate + 2 wt% NaCl addition	Salt-rich phase K = 25	[58]

Table 1 (*continued*)

Compound	ABS	Description	Optimal conditions	Results	Ref.
strong antioxidant capacity. Used as food supplements and additives.		ABS composition, sample load, pH and adjuvants (NaCl and ILs) were studied.	pH 8, 5 wt% of 1 mg/mL sample loading		
Vitamin B6 *Displays a central role in amino acid metabolism and modulating the activity of many hormones. Used as an additive in different foods.*	**Alcohol + organic solvent — salt** (EtOH + isopropyl alcohol/ PMG), (Na_2SO_4, Na_2CO_3 NaH_2PO_3)	Quaternary ABS composed of (PMG/isopropyl alcohol), ethanol, salt (Na_2SO_4/Na_2CO_3) and water were investigated as a detection system for vitamin B6. Binodal curves were designed for systems and temperature, alcohol and salt concentration effects on binodal curves and tie-lines were evaluated. Then, extraction of vitamin B6 was studied.	isopropyl alcohol + EtOH + Na_2CO_3 35°C, pH 5	Salt-rich phase EE ≈ 89%	[59]
Application B — ABS as an analytical tool					
Artrazine, methylene blue and sudan III *Synthetic dyes. Used as colorants in food industry.*	**DES — DES** (HFIP-based and PPG 400-based hydrophobic DES), ([Ch]Cl based hydrophilic DES) (*cf.* [60] for more details)	Hydrophillic and hydrophobic DESs were combined to form ABS. By manipulating the hydrophobicity of systems, partition of dyes was studied. Single factor experiments were performed to optimize temperature, ionic strength (addition of NaCl), dye mass and pH. Real samples and mixed dye samples were tested. Recycling of phase pharming components and extraction mechanism were also studied.	$[N_{4,4,4,4}]Br$ — PPG 400 (6 wt% water) + ChCl — glycerol (23 wt% water)	Hydrophilic DES-rich phase Tartrazine EE ≈ 89% Methylene blue EE ≈ 93% Hydrophobic DES-rich phase Sudan III EE > 83% LOD — 34 ng mL^{-1}	[60]
Proteins *Present in traces in oils and can be problematic for individuals who are allergic to proteins. Oil proteins have been used as food supplements and emulsifiers.*	**IL — salt** ($[C_4mim]Br$ $[C_6mim]Br$ $[C_2mim]Br$ $[C_2mim]Cl$ $[C_4mim]Cl$ $[C_6mim]Cl$) (K_3PO_4, KH_2PO_4, K_2CO_3)	Several different ABS were used for extraction of proteins from edible oil for rapid detection. Biphasic curves were designed for all systems. Extraction in all systems was screened and optimal conditions (system composition, temperature, and pH) were determined for the most promising one. At the end, system was applied to real samples.	20% (w/v) $[C_4mim]Cl$ + 50% (w/v) K_3PO_4 35°C, pH 9	IL-rich phase EE ≈ 100% K ≈ 90	[61]
Cadmium and manganese *Cadmium is a toxic metal that can be a contaminant in food and can cause health problems when ingested even in low concentrations. Manganese is essential for organisms and is important for biological processes; however it can cause alterations in*	**Polymer — salt** (PEG 1500, 4000, 6000), (K_2HPO_4)	Cadmium and manganese in food samples were detected with the aid of ABS. Doehlert matrix was then applied to find the optimal conditions (namely, pH and molecular weight) for extraction process. Later extraction time, mass ratio of phases and tie-line length were optimized and process was applied to green tea and soluble coffee samples.	Tie-line length = 53.3%w mass ratio between bottom and top phases: 0.029 18 hours extraction time	Cd Rec. ≈ 98% LOD — Mn Rec. ≈ 99% LOD — Cd: 0.45 ng kg^{-1} Mn: 6.4 ng kg^{-1}	[62]

Table 1 (*continued*)

Compound	ABS	Description	Optimal conditions	Results	Ref.
central nervous system under prolonged exposure.					
Triazole fungicides *Broad-spectrum fungicides used in the control of fungal diseases in different plants. Cannot be present in food products.*	**Copolymer — IL** (ethylene/propylene oxide copolymer 2500) ([Ch][Ac], [Ch][D-Lac], [Ch][L-Lys], [Ch][D-Ser], [Ch][L-Ser])	ABS was coupled with high-performance liquid chromatography in order to detect enantiomers of myclobutanil and tebuconazole in fruit juice. Binodal curves were designed. After screening, process conditions were determined for the best one.	25 wt% [Ch][L-Lys] + 25 wt% copolymer	Copolymer-rich phase Rec. ≈ 80–89% LOD — 0.1–1 μg kg^{-1} LOQ — 0.5–5 μg kg^{-1}	[63]
Nine different pesticide residues *Different pesticide residues are used for pest control. Cannot be present in food products.*	**Alcohol — salt** (EtOH), (K_2HPO_4)	Pesticide residues were detected in food samples. Ultrasonic-assisted aqueous biphasic extraction was coupled with vortex-assisted dispersive liquid–liquid microextraction. Optimal conditions were determined for the tested system.	30 wt% EtOH + 25 wt% K_2HPO_4 15 min, 70°C	Alcohol-rich phase Rec. ≈ 77–99% LOD — 5.6–17.4 μg L^{-1} LOQ — 18.6–50.1 μg L^{-1}	[64]
Application C — ABS as *in situ* bio-based platforms					
Laccase *Multicopper oxidase capable of oxidizing a large number of phenolic and nonphenolic molecules. Used for wine stabilization, baking, and flavoring.*	**IL — salt** **IL — polymer** **Polymer — salt** **Polymer — polymer** (long list of compounds — *cf.* [65] for more details)	Some binodal curves were designed while others were used from literature. Screening of imidazolium-, pyridinium-, pyrrolidinium-, piperidinium-, tetraalkylphosphonium-, and tetraalkylammonium-based ILs in ternary and quaternary ABS, as phase-forming compounds or adjuvants, respectively, for the extraction of laccase and their effect upon the enzyme activity.	Ternary ABS: 12 wt% [Ch][DHC] + 48 wt% PPG 400 Quaternary ABS: 27 wt% PPG 400 + 5 wt% K_2HPO_4 + 3 wt% [Ch][DHC]	Laccase migrates preferably towards the most hydrophilic phase, that is, IL-rich phase Ternary ABS: EE = 100% $Act_{Laccase}$ ≥ 1000 U L^{-1} Quaternary ABS: EE = 100% Rel. $Act_{Laccase}$ ≥ 150%	[65]
Laccase and Remazol Brilliant Blue R (RBBR) *Remazol brilliant blue is a dye used in textile industry and toxic when present in water.*	**IL — polymer** **Polymer — salt** **Polymer — polymer** ([Ch][DHC], [Ch][DHP], [Ch][Ac]), (K_2HPO_4), (PEG 400, PPG 400)	IL-polymer ABS were evaluated as liquid support for laccase and compared with polymer–salt and polymer–polymer ABS. Most promising ABS were used to determine laccase catalytic performance to decolorize dyes. Recycling studies were evaluated.	46 wt% PPG 400 + 16 wt% [Ch][DHC] + 29 wt% laccase solution + 8.97 wt% H_2O + 0.03 wt% RBBR	IL-rich phase Laccase EE ≈ 100% $Act._{Laccase}$ ≈ 100–60%, after 6 cycles Polymer-rich phase RBBR and degradation products EE ≈ 100% (≈ 96% after 6 cycles)	[66]
Rutin *Flavonoid present in fruits and vegetables with antioxidant properties. Used as a nutraceutical.*	**IL — polymer** ([CH][DHP], [Ch][Ac], [Ch][Gly], ([Ch][DHph]), (PEG 600)	Laccase-catalyzed oligomerization of rutin was performed within the ABS under homogenous and heterogenous media. Recycling studies were evaluated. A life cycle assessment also performed.	Heterogenous medium: 26.1 wt% of PEG + 26.7 wt% of [Ch][DHP] + 47.2 wt% H_2O* *Includes: Laccase catalytical activity = 1000 U L^{-1} Initial rutin concentration = 3 g L^{-1}	Polymer-rich phase Rutin/oligorutin Oligomerization yield ≈ 95% (≈ 89% after 3 cycles) $EE_{oligorutin}$ = 65–67% IL-rich phase Laccase Rel. Act. ≥ 70% $EE_{laccase}$ ≥ 93%	[67]
Anthocyanin *Bioactive food compound. Used in the food industry as interfacial assembly polymer.*	**Polymer — polymer** **Polymer — protein** **Polymer + protein — polymer** (collagen+pectin) — chitosan	Development of alternative polymer–polymer and polymer–protein ABS. Design of binodal curves. Formation of ABS-based microcapsules for anthocyanin encapsulation.	(4 wt% collagen + 0.5 wt% pectin) + 1 wt% chitosan + 94.5 wt% H_2O pH 6	Encapsulation efficiency ≈ 93% Loading capacity ≈ 12.3 g 100 g^{-1}	[68]

Table 1 (*continued*)

Compound	ABS	Description	Optimal conditions	Results	Ref.
Bacteriocin-like inhibitory substances *Act as preservatives in different foods.*	**Polymer — polymer** (PEG 2000, 4000, 6000, and 8000), (dextran T500)	ABS was developed simultaneous cell cultivation and downstream processing of bacteriocin-like inhibitory substances. Activity was tested in all studied systems, and factorial design was applied for optimization od process parameters. After product migrated to PEG-rich phase, dextran-rich phase containing cells was recycled, while acetone was added to the PEG-rich phase in order to precipitate the desired compound. Scale-up was applied at optimal conditions.	10 wt% PEG 2000 + 8 wt% dextran T500 pH 7, 200 rpm	PEG-rich phase Yield ≈ 77%	[69]
Fungal pigments *Used as natural colorants.*	**IL — salt** ($[N_{4,4,4,4}]Br^-$, $[C_4mim]Br^-$, $[C_4mim]Cl^-$), (Na_2CO_3 and $Na_2CH_3CO_2$)	Extraction of pigments from fermentation broth. Binodal curves were designed in order to study different IL-salt ABS. Systems were then applied to fermentation broths to study extraction abilities of these processes. After target molecules moved to IL-rich phase, backextraction was performed and IL phase was reused.	15 wt% $[N_{4,4,4,4}]Br$ + 25 wt% $Na_2CH_3CO_2$ + 60 wt% fermented broth	IL-rich phase Red colorant EE > 99% K > 1000 Orange colorant EE > 99% K > 1000 Yellow colorant EE > 99% K > 300	[70]
3-Poly-L-lysine *Used as a natural food preservative.*	**Alcohol — salt** (MeOH, EtOH, acetone, ethyl acetate), ($(NH_4)_2SO_4$, NaH_2PO_4, KCl, NaCl, Na_3PO_4)	Several different ABS were screened. Phase diagram was designed for the most optimal system, which was studied in more detail. Later, multistage extraction was performed from fermentation broth and the product was purified using ultrafiltration.	20 wt% EtOH + 20 wt% $(NH_4)_2SO_4$ + 60 wt% fermented broth pH 9.5	Alcohol-rich phase Rec. ≈ 96% K = 18.36	[71]
Application D — Valorization of food waste using ABS					
Polysaccharides *Seedcakes are by-products of squeezing oil.* *Used as stabilizers, thickening agents, emulsifiers and humectants.*	**Copolymer — DES** (ethylene oxide-propylene oxide (EOPO) 2000, 2500 and 3000), ([Ch]Cl–ethylene glycol)	Seed cake was used as a source for extraction and preliminary purification of polysaccharides. DES was used for extraction and thermosensitive ABS composed of copolymer and DES for purification. First, different DESs were screened; conditions (water percentage, SLR, temperature, time and pH) were optimized for the best one. Two-step ABS was then used for separation of the product. During the first step, polymer molecular weight, concentration, and temperature were optimized. The second step was temperature induced phase separation for recovery of the product and copolymer.	60 wt% EOPO 2500 + 40 wt% ChCl-ethylene glycol (30% water) 40°C	Copolymer-rich phase 1st step: EE ≈ 87% 2nd step: Rec. ≈ 85%	[72]
5-HMF *Apple peel waste was used as a source of fructose.*	**DES — salt** ($[N_{4,4,4,4}]Cl$:EtOH, $[N_{4,4,4,4}]Cl$:n-propanol), (K_3Cit)	5-HMF was extracted from apple peel waste using switchable pH-driven ABS. Phase diagrams were	30 wt% $[N_{4,4,4,4}]Cl$:EtOH (1:2) + 35 wt% K_3Cit 30 wt% $[N_{4,4,4,4}]Cl$:n-propanol (1:2) + 40 wt% K_3Cit	DES-rich phase 5-HMF: Yield ≈ 47% EE ≈ 99%	[73]

Table 1 (*continued*)

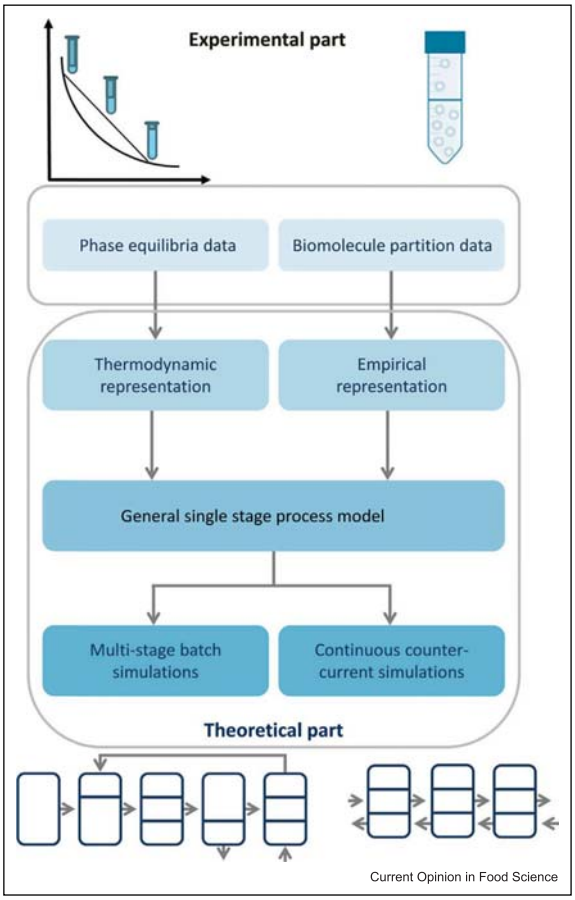
Compound	ABS	Description	Optimal conditions	Results	Ref.
		designed. Fructose conversion to 5-HMF was done in DES in presence of citric acid, and then KOH was added. Because of pH change, biphasic system formed and 5-HMF partitioned to DES-rich phase, while fructose moved to salt-rich phase. Conditions were optimized.		Salt-rich phase Fructose: Conversion rate ≈ 87%	
Phenolic antioxidants *Used as antioxidant agents.*	**Polymer — salt** (PEG 600, 1000, 4000), (Na_3Cit)	Antioxidants were recovered from *Garcinia mangostana* pericarps. Different surfactants were added to the ABS to improve its efficiency. After, PEG molecular weight, volume ratio, sample loading and pH were tested, one after the other (fixing optimal parameter at each step). At the end, surfactant concentration was optimized.	21 wt% PEG 1000 + 17 wt% Na_3Cit + 1 wt% Tween 85 pH 8, 0.2 wt% sample loading	Polymer-rich phase Yield ≈ 95% K = 12.42	[74]
Caffeine, taurine, and niacin *Caffeine is an alkaloid used in food industry as a stimulating drug Taurine and niacin are dietary supplements.*	**IL — polymer** ([Ch]-based: [Lac], [Tau], Cl, [Ac], [DHP], [Pyr], [Nia]), (PPG 400)	Expired energy drinks were used a source of caffeine, taurine, and niacin. Binodal curves designed for different IL — PPG 400 ABS which were applied for extraction. Cytotoxicity and ecotoxicity of different ILs were tested. Recovery was measured in different ABS compositions.	30 wt% [Ch][Nia] + 30 wt% PPG 400 + 40 wt% water 25°C	IL-rich phase Rec. > 82%	[75]
Ascorbic acid and vanillin *Ascorbic acid and vanillin are flavoring agents.*	**Alcohol — salt** (EtOH), (K_2HPO_4)	Ascorbic acid and vanillin were extracted from diet pudding waste. Optimal ABS was presented in previous study published by the same group. Semicontinuous and continuous systems were tested. Single factor experiments were performed for flow rate and agitation speed optimization.	50 wt% EtOH + 15 wt% K_2HPO_4 + 35 wt% H_2O Semicontinuous operation at 25°C, 60 rpm and 6 mL min^{-1}	Alcohol-rich phase Vanillin: Rec. ≈ 94% K = max. Salt-rich phase Ascorbic acid: K = 0.023	[76]
Bioactive compounds (soluble phenols, flavonoids, anthocyanins and condensable tannins)	**Polymer — salt** (PEG 4000), (Na_3Cit, $MgSO_4$)	Several different bioactive compounds present in avocado residue waste were extracted using ABS. Binodal phase diagrams were developed. Partition and antioxidant activity were evaluated.	24.9 wt% Na_3Cit, 14.5 wt% PEG 4000 12.2 wt% $MgSO_4$, 15.5 wt% PEG 4000	90% efficiency compared to methanol process Rec. > 82%	[77]
Lipase *Used as flavor enhancers.*	**Copolymer — salt** (poly(ethylene glycol-ran-propylene glycol) monobutyl ether (EOPO)) (Na_2HPO_4, K_2HPO_4, $Na_3C_6H_5O_7$, $(NH_4)_2SO_4$)	Thermoseparating ABS were applied to extract lipases from fish residues. The first step was screening of several systems at different conditions to find the most promising one. In the second step, water was added to recovered copolymer-rich phase in order to purify the product and recycle the components. During the recycling step, lipases from	First step: 40 wt% EOPO 3900 + 10 wt% $(NH_4)_2SO_4$ + 4 wt% NaCl + 20 wt% crude enzyme Second step: 50 wt% copolymer + 50 wt% water 60°C	Copolymer-rich phase Yield ≈ 94% 1st step: K = 0.49 2nd step: water/lipase-rich phase	[78]

Table 1 (*continued*)

Compound	ABS	Description	Optimal conditions	Results	Ref.
		the salt-rich phase were also recovered.			
Flavonoids (rutin, quercetin 3-β-D-glucoside, and kaempferol-3-O-rutinoside) *Used as antioxidants and food supplements.*	**Alcohol — salt** (EtOH), (K_2HPO_4)	Jujube peel waste was the source of different flavonoids. After binodal curves were designed, screening was used to design Box-Behnken experiment with four variables, namely salt concentration, SLR, ultrasonic power and extraction time. At the end, extraction mechanism was studied in more detail.	20 wt% EtOH + 35 wt%, K_2HPO_4 SLR 0.03 g/mL^{-1} ultrasonic power 200 W, 50 min	Alcohol-rich phase Rec. ≈ 97% K = 392	[79]
Protein *Used as a source of amino acids.*	**Polymer — salt** (PEG 2000), (Na_3Cit)	Herein shrimp waste was used as a source of protein. Binodal curves were designed and response surface methodology was coupled genetic algorithm/particle swarm optimization to optimize protein extraction, variables being PEG and salt concentrations, pH and temperature.	15.8 wt% PEG 2000 + 16 wt% Na_3Cit pH 8, 25°C	Polymer-rich phase Yield ≈ 95%	[80]
Alternative liquid–liquid systems					
Fipronil and its metabolites *Broad-spectrum insecticide and its metabolites are used in pesticide control. Cannot be present in food products.*	**Organic solvent — water** (acetonitrile)	Cold-induced ABS was coupled with liquid chromatography–high resolution mass spectrometry to detect fipronil and its metabolites in dietary samples. Analyte was enriched and separated from lipids in acetonitrile phase. ABS conditions were optimized.	50 wt% acetonitrile + 50 wt% water 60 min	Nitrile-rich phase Rec. ≈ 89–100% LOD — 3–5 ng kg^{-1} LOQ — 10–30 ng kg^{-1}	[81]
Nine Mycotoxins *Fungi products causing disease in humans and animals. Cannot be present in food products.*	**Alcohol — salt** **Organic solvent — salt** (EtOH), (acetonitrile), ($(NH_4)_2SO_4$)	Ultrasonic-assisted ABS combined with backextraction was used in a tandem with HPLC to detect toxins in different samples. After screening of several ABS, optimal conditions were determined by single-factor experiments.	34 wt% acetonitrile + 22 wt% $(NH_4)_2SO_4$ 40°C, pH 6, 10 min	Organic solvent-rich phase Rec. ≈ 98% LOD — 0.01563–0.5161 ng mL^{-1} LOQ — 0.05210–1.720 ng mL^{-1}	[82]
Thiocyanate *Used in small concentrations for prolonging milk shelf-life through the lactoperoxidase system. Toxic for humans through excessive addition. Cannot be present in food products.*	**Organic solvent — salt** (acetonitrile, acetone), ($(NH_4)_2SO_4$)	Method to detect thiocyanate in milk was herein proposed. Response surface methodology was applied to optimize determination efficiency of the process. After ABS was chosen, anion-exchange column for separation and an amperometric detector or ultraviolet detector for determination were used.	42 wt% acetonitrile + 16 wt% $(NH_4)_2SO_4$, pH 4.7	Organic solvent-rich phase Rec. ≈ 107% LOD — 0.2 μg L^{-1} LOQ — 0.6 μg L^{-1}	[83]

Abbreviations: K – partition coefficient, PF — purification factor, PEG — polyethylene glycol, SLR — solid–liquid ratio, PPG — polypropylene glycol, BSA — bovine serum albumin, IgG — immunoglobulin G, Cyt C — cytochrome C, P_{NE} — copolymer of N-isopropylacrylamide + ethyl methacrylate, $P_{ADB4.91}$ — copolymer of acrylic acid +2-(dimethylamino) ethyl methacrylate, P_{NDBN} — copolymer of N-isopropylacrylamide +2-(dimethylamino) ethyl methacrylate, Rel. Act — relative activity, 5-HMF — 5-hydroxymethylfurfural.

Figure 3



Overview of multiscale modeling framework with experimental and theoretical data being correlated.
Adapted from Ref. [111].

with experimental data to understand and control food protein structure and function [113].

Concerning simulations within DSP, molecular dynamics is a remarkable example of a computational tool capable of giving nanoscale and subnanoscale detailed insights into the phenomena underlying ABS [114] and their applications, including the polyphenolics [56] and enzyme [111] extractions, commonly required in food industry. Moreover, molecular docking can later be used to understand the underlying interactions between the biomolecules and the ABS constituents [25,115].

Currently, there are scarce works combining simulation and experimental studies regarding the influence of the ABS-phase formers upon the biomolecule's extractive performance [111,116]. Nevertheless, these studies were able to develop dynamic process models that can better understand the behavior of ABS and predict the process behavior of DSP. Moreover, two machine-learning models have just been developed to predict the phase composition of polymer–electrolyte ABS and the partition performance of biomolecules [117].

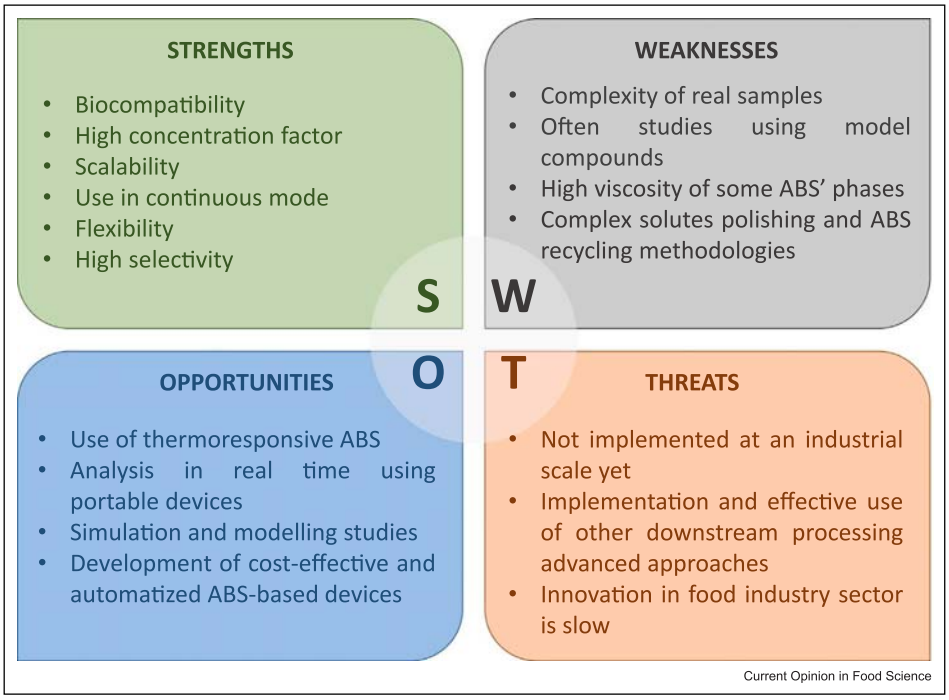
Overall, we anticipate that dynamic modeling and computational tools will be crucial to predict and understand the underlying mechanisms dictating different process units within an industrial platform as well as maximize the outputs by correlating experimental and theoretical data (*cf.* Figure 3).

Critical perspective

The broad versatility of ABS for food processing was here presented. It is true that most studies still regard the application of ABS as an advantageous alternative in DPS to obtain food-related biomolecules and as concentration tools for analytical quantification. Yet, emerging approaches have also been proposed. The possibility of using ABS as *in situ* bio-based platforms for biocatalytic processes is an innovative approach, especially considering their simultaneous use as liquid supports for enzymes and biocompatible reaction media. For instance, the sustainability and the cost-effectiveness of the process are ensured as the ABS as liquid supports allow the enzyme reuse without considerable losses, while guaranteeing the product isolation in the opposite phase. Considering that the use of enzymes in food processing is a crucial step in many technologies, further studies on this topic are worth pursuing, namely the use of continuous and integrative platforms at larger scale. Moreover, ABS have shown great potential for loading and delivery of hydrophilic bioactive ingredients, which outperformed even the conventional systems. Thus, encouraging further investigation in fully food-grade-based ABS that can potentially be used in formulations.

When considering the intensified increase in world population and, consequently, the tackling pressure to increase food production, a considerable rise is also expected in the production of food waste. In the meanwhile, there is the imperative switch toward a circular economy approach that demands the reduction of waste being generated, and if its generation is unavoidable, its use as feedstocks for new chemicals/products is recommended. Therefore, several studies have proposed the use of food waste as raw materials for different products, in which ABS can be the key step for developing sustainable strategies for food waste valorization. Owing to the multitask capacity of ABS, we believe that these can even be used to combine the solid–liquid and LLEs commonly applied. However, these studies still lack the inclusion of a full biorefinery approach with process integration, continuous processing, recyclability/reusability, and scale-up analyses not to even mention a life cycle assessment and a techno-economics analysis

Figure 4



SWOT analysis of ABS for food processing.

that are vital to ascertain the industrial feasibility of the technology. Hence, leaving multiple opportunities for new studies.

As a final remark, we present our view regarding the ABS strengths, opportunities, weaknesses, and threats for food processing, through the SWOT analysis presented in Figure 4.

Conflict of interest statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

All data discussed have been disclosed in the paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.cofs.2023.100991.

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