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Novel extraction of bioactive compounds from algae using green solvent: Principles, Applications, and Future perspectives

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ABSTRACT

Bioactive compounds, such as phenolics, terpenoids, and fatty acids, are essential for pharmaceutical and health care applications; however, the extraction of these compounds from algae is challenging because of their low polarity and rigid cell walls. The applications of novel extraction techniques using green solvents have been widely researched because of the rising demand for sustainable production. This work aims to review novel extraction techniques, such as ultrasonic-assisted, microwave-assisted, enzymatic-assisted, and supercritical fluid extraction, using green solvents to recover bioactive compounds from algae. This review presents (i) the principles of using green solvent-based novel extraction techniques, (ii) the effect of extraction conditions on the overall yield of bioactive compounds, (iii) and the applications of green solvent-based extraction techniques in recovering bioactive compounds from algae. The metadata analysis is conducted to compare the extraction efficiency of those novel extraction techniques. Microwave-assisted extraction (MAE) shows the highest recovery efficiency (70 mg/g) in recovering the bioactive compounds among the four techniques. The data of novel extraction techniques will provide strong support for designing and practicing the extraction of bioactive compounds at an industrial scale. The review also proposes hybrid extraction techniques to improve the extraction yield of bioactive compounds. MAE can be combined with ultrasonic-assisted extraction, supercritical fluid extraction, and enzyme-assisted extraction, in which MAE acts as the pretreatment method.

1. Introduction

Algae are an essential food source in several countries, such as America, Vietnam, China, and South Korea [1]. There are over 30 thousand algal species, of which 50 types are suitable for human consumption [2]. Algae are classified based on their sizes (macroalgae and microalgae) or their colors, such as green, brown, and red algae [2]. Several algae having photosynthesis capability, such as *Dunaliella salina*, *Spirulina plantensis*, and *Chlorella vulgaris,* can be considered edible algae [3]. Currently, edible algae are a source of bioactive compounds (BCs) in Europe and America as they are a rich source of nutrients, pigments, and antioxidants.

BCs are secondary metabolites of algae, given that they participate in the defense mechanisms to prevent the attack of herbivores [4]. The secondary metabolites also promote the communication of aquatic species with others and protect them from extreme environmental conditions, such as ultraviolet radiation. BCs consist of several main groups: amino acids, phenolic compounds, terpen and terpenoid compounds, alkaloids, fatty acids, and polysaccharides [5]. These compounds play a critical role in improving human health, such as alleviating the development of cardiovascular risk and showing anti-inflammation and anti-neurological degeneration [6]. Thus, the demand for consuming BCs is increasing, which urges the sustainable production of these compounds at the industrial scale. Mass-scale manufacturing of BCs is restricted by the limit of raw materials and biomass supply [5]. This problem can be solved by sustainable

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extraction techniques using green solvents.

Extraction is the recovery process of BCs from algae, followed by purifying crude extracts [7]. The traditional extraction techniques for recovering BCs are maceration, hydrodistillation, mechanical pressing, and steam distillation [7]. However, these approaches have several limitations, such as low extraction yield, extensive extraction time, and high quantity of solvent volume required. Novel extraction techniques, such as microwave, enzymatic, ultrasonic, and supercritical fluid extraction, can address the afore mentioned limitations. The improvements in extraction techniques are less chemical intensive, highly efficient, low-cost, and sustainable. The extracts obtained by these techniques can be employed in food products as food additives and preservatives [8]. The enriched-bioactive component extracts from brown algae are added as a functional ingredient in juices, meat, dairy, bakery, and pasta products [9].

Solvents are essential to the extraction procedures since they separate the soluble fraction of interest in the algal matrix and purify the obtained extracts [10]. The high consumption of organic solvents raises environmental issues, such as volatile organic pollution and waste. Reducing organic solvent usage or substituting them with green solvents is an essential alternative. The novel extraction process can decrease organic solvent consumption, while a new class of solvents, such as water, ionic liquids, deep eutectic, supercritical, subcritical, and bio-based solvents, have been developed [10]. A new class of solvents is considered green solvents when they conform to the rules of green chemistry, such as less hazardous chemical synthesis, safer solvents and auxiliaries, design for energy efficiency, and design for degradation [11]. For example, a supercritical fluid is used to extract the metabolites from algae, and the research also investigated the effects of algal extracts on human health [12].

The novel extraction techniques for recovering BCs have been reviewed extensively in marine algae, subcritical water extraction of algal components, and supercritical fluid extraction of natural compounds [13–15]. However, novel extraction techniques such as ultrasonic-assisted extraction (UAE), microwave-assisted extraction (MAE), enzymatic-assisted extraction (EAE), and supercritical fluid extraction (SFE) combined with green solvent in extracting BCs from algae have not been considered. In addition, the previous studies did not conduct metadata analysis to compare the extraction yield of BCs from different novel extraction techniques. Therefore, a critical review of novel extraction techniques in conjunction with green solvents towards sustainable production is critically needed. In this review, we will cover (i) the principle of novel extraction techniques, (ii) the effects of extraction conditions on the recovery yield of BCs, (iii) the applications of these techniques in extracting natural compounds from algae, and (iv) metadata analysis to compare the extraction yield of four extraction techniques.

2. Bioactive compounds in algae

BCs refer to an extended array of biochemical substances extracted from algae, such as amino acids, phenolics, terpenes and terpenoids, alkaloids, fatty acids, and polysaccharides. This review will focus on three main groups: phenolics, terpenoids, and fatty acids.

2.1. Phenolics

Phenolic compounds are widespread in algae as they are vital to algae growth and survival. They are synthesized from phenylpropanoid, pentose phosphate, and shikimate pathways [16]. The general structure of phenolics consists of an aromatic ring containing one or more hydroxyl groups. The molecular weight of the phenolic molecules can vary from a hundred to a thousand dalton. In nature, phenolic compounds preferentially form a complex with sugar, polysaccharides, esters, methyl esters, and other phenolics.

Phenolic acids, flavonoids, and tannins are the classes of phenolic compounds in algae suitable for human consumption. Phenolic acids are composed of at least one aromatic ring, in which a hydroxyl group replaces one hydrogen atom. The basic structure of flavonoids is C_6–C_3–C_6, consisting of two aromatic rings A and B. The two rings are linked via the heterocyclic ring C, which takes responsibility for flavonoid diversity. The changes in C rings result in the generation of flavonoid sub-classes, such as flavonols, flavanonols, flavanones, flavones, isoflavones, flavanols (catechins), and anthocyanidins. The flavonoid compounds are complex when stored in algae as an energy reserve [17].

Tannins are the polymer of tannic acids and are categorized into hydrolyzable and condensed tannins. Hydrolyzable tannins are derived from shikimate, while condensed tannins are the polymers and oligomers of flavan-3,4-diols and flavan-3-old [17].

2.2. Terpenoids

Terpenoids are known as isoprenoids, which are one of the most popular groups of natural substances. Terpenoids are modified terpenes, where oxygen atoms substitute methyl groups, or the carbon skeleton is changed by oxidation. Terpenoids are commonly categorized into seven groups. Mono-, sesqui-, di-, and sesquiterpenes have the isoprenoid monomers connected by a head-to-tail pattern. The triterpenoids and carotenoids (tetraterpenes) have two C_{15} and C_{20} units, in turn, connected via a head-to-head pattern [18]. Carotenoids are the most widespread terpenoid classes in macro and microalgae, such as *H. rubicundus*, *Bracteacoccus aggregatus*, *Haematococcus lacustris*, and *Coelastrella aeroterrestrica*. Based on the presence of an oxygen atom in the chemical formulation, carotenoids are classified into two main groups: carotenes and xanthophylls. The common carotenes encompass lycopene and α-carotene, β-carotene, while astaxanthin, torularhodin, lutein, canthaxanthin, violaxanthin, zeaxanthin, and fucoxanthin are the popular xanthophylls in algae [19].

2.3. Fatty acids

Fatty acids are the main metabolic substances generated from acetyl coenzyme A. The chemical structure of fatty acid has two main parts: the carboxylic acid group at one end and the hydrocarbon chain with a methyl terminal [20]. The carbon atom next to the carboxyl group is designated the alpha (α) carbon, while the methyl terminal is called the omega or n carbon in their nomenclature [20].

Fatty acids are classified as saturated, monounsaturated, and polyunsaturated according to the number of double bonds in their chains. Saturated fatty acids are myristic, stearic, and palmitic, while monosaturated and polyunsaturated fatty acids are oleic and docosahexaenoic, respectively [20]. Docosahexaenoic acid (DHA) has 22 carbons and six double bonds in its chain, and it is described as 22:6 n-3. Docosahexaenoic acid and eicosapentaenoic acid (EPA) commonly occur in algal species, such as *Phaeodactylum tricornutum*, *Nannochloropsis oculata*, *Seminavis gracilenta*, *Isochrysis galbana*, and *Prorocentrum minimum* [21].

3. Green solvents used in bioactive compound extraction from algae

3.1. Water and subcritical water

Water is considered a green solvent because it conforms to the principles of green chemistry. Water has a high dielectric constant of 78.3, which can be ascribed to its dipole orientation of hydrogen bond networks. The water polarity is substantially reduced at high pressure and temperature due to the disintegration of hydrogen bond networks. Water has been employed to extract natural compounds from plants; however, it merely recovers high and semi-high polar compounds [22].

Subcritical water is the special phase of water under specific pressure and temperature, which ranges from boiling to critical points. Water

remains in the liquid state at specific conditions where temperatures significantly affect water polarity. Due to decreased water polarity, the organic molecules are more soluble at subcritical conditions. The decrease in water polarity can be calculated from its dielectric constant. For instance, water polarity at 214 °C and 295 °C is similar to methanol and acetone at ambient temperature [23]. Therefore, subcritical water is commonly used to recover the low and non-polar compounds from algae.

3.2. Deep eutectic solvents (DES)

The deep eutectic solvents are considered one subclass of the ionic liquids [24]. DES is synthesized by blending the hydrogen bond donors (HBD) and hydrogen bond acceptors (HBA) at determined molar ratios. The freezing points of DES are lower than each ingredient because the hydrogen bond networks between HBA and HBD are generated [25].

Natural deep eutectic solvents (NADES) are the subclass of DES in which natural metabolites in cells, such as organic acid and polyol, are used as HBA and HBD. The advantages of NADES over ionic liquids are easy storage, simple synthesis, and low-cost production. NADES viscosity is usually high at ambient temperatures, resulting from the high expanded hydrogen bond networks. The NADES viscosity is mainly affected by the density of hydrogen bond networks, water content, and steric effects (hole theory). The occurrence of holes or voids in the liquid can impact liquid viscosity. NADES has numerous tiny holes that are more vicious, leading to the restriction of ionic motion [26]. The surface tension of NADES is high because of their high viscosity [26]. In addition to viscosity, the surface tension of NADES is affected by HBD, in which the high quantity of hydroxyl groups and long alkyl chains can result in high surface tension. The polarity of NADES is the key criterion because it describes the overall solvation capability.

3.3. Bio-based solvents

Bio-based solvents are usually generated from agricultural biomass and are categorized into four groups: sugar and starch; (2) lignocellulosic; (3) protein and oil-based, and (4) other forestry and food wastes, whose classifications are based on the origin of agricultural biomass, employed for solvent generation. The solvents acquired from these classes can be categorized according to their functional groups (esters, terpenes, ethers, and alcohols). Bio-based solvents should conform to the twelve principles of green chemistry. The solvents should stem from renewable feedstocks, be recyclable using green processes, and show similar attributes as organic solvents, high boiling temperatures, biodegradability, and low vapor pressure [22]. The production of bio-based solvents should not negatively affect the natural environment.

4. Novel extraction techniques suitable with green solvents

Algal cell walls are composed of a mix of biomolecules, such as sulfated and branched polysaccharides, which are linked to proteins and bound ions like calcium and potassium [13]. To extract bioactive compounds from algae, it is necessary to break down these complex molecules of the cell walls. Common treatments to degrade algal cell walls are enzyme-assisted extraction (EAE), microwave-assisted extraction (MAE), ultrasonic-assisted extraction, supercritical fluid extraction (SFE), and pressurized liquid extraction (PLE). Along with their advantages, each method has its drawbacks when being utilized for algal extraction. Although EAE has the highest selectivity, it can be time-consuming to allow the enzymes to react with the target substances. Additionally, the use of enzymes requires strict operating conditions due to the sensitivity of enzymes to changes in temperature, pH, ionic concentration, etc. As MAE can increase the temperature of the medium, it is not suitable to attain thermolabile compounds. In UAE, wave attenuation can occur and reduce the extraction efficiency. Regarding SFE, it requires high-cost instruments, which can limit the use of this method. The low polarity of supercritical CO2 also hinders the use of SFE for compounds that have high polarity. Due to the extracting mechanism of PLE, it is not suitable to attain compounds that are sensitive to high temperature and high-pressure conditions. Furthermore, certain extracting methods require an additional step of purification to isolate target compounds from the others (cell wall fractions, solvent, etc.). Additionally, the extraction of undesired bioactive compounds from algae with similar solubility can also take place, which reduces the purity of the extraction yield. To address this issue, several approaches have been developed. For instance, when isolating fucoidan, pretreating the algae with a methanol/chloroform/water mixture at a ratio of 4:2:1 (v/v/v) has proven beneficial in preventing the coextraction of other algal substances during the aqueous extraction process [27].

Putra et al. conducted an optimization of the ultrasound-based technique to extract phenolics from red algae by examining the temperature, solvent concentration, pulse duty cycle, ultrasound power, and solvent-to-sample ratio [28]. After optimizing these factors, the phenolic contents yielded from *Kappaphycus alvarezii* was 845.28 ± 93.17 mg GAE/kg, which was significantly higher than the yield prior to the optimization (below 400 mg GAE/kg).

Safari et al. employed response surface methodology to find out the optimum microwave-based conditions for the extraction of antioxidant compounds from the Persian gulf green algae (*Chaetomorpha* sp.) [29]. For instance, decreasing acetone concentration from 75 % to 25 % caused an increase in the phenolic yield. Meanwhile, when increasing treatment time from 6 to 8 min, the ferric reducing power increased significantly. Additionally, an increase in microwave power led to an increase in DPPH radical scavenging activity. After optimizing the conditions of solvent concentration, microwave time and power, they attained maximum recovery (total phenolic content: 0.98 mg tannic acid/gram dry weight algae; ferric reducing power: 0.086 mg tannic acid/gram dry weight algae; DPPH radical scavenging ability: 99.38 %; and total ascorbic acid content: 0.16 mg ascorbic acid/gram dry weight algae) with less energy (300 W of microwave power), solvent consumption (25 % acetone) and extraction time (8 min).

Mäki-Arvela discussed the effect of several extracting parameters on the extraction of carotenoids from algae [30]. When applying pressurized-liquid extraction, typically, a longer extraction time facilitates a higher extraction yield. However, in some cases, for example, in the extraction of lutein, a longer time resulted in a lower yield. The effect of temperature can either be very dominant or exhibit only a minor effect, and some combinations of temperature and time can cause side reactions. In a study by Shang et al., the optimum extraction temperature for fucoxanthin from fresh *Eisenia bicyclis* with 90 % ethanol was 110 °C during 5 min of extraction time [31]. One limitation of employing higher extraction temperatures, such as in the extraction of lutein and β-carotene from *Chlorella vulgaris*, is the conversion of chlorophyll a into pheophorbide. The formation of pheophorbide increased over time but peaked at 60 °C, after which it declined as the temperature continued to rise, as chlorophyllase is deactivated at high temperatures [30].

In summary, it is crucial to optimize the extracting parameters in order to attain the highest yield while still maintaining the integrity of the target compounds from algae. Additionally, saving the cost of energy and solvent consumption is also important when optimizing the extraction system.

4.1. Ultrasonic

Ultrasonic-assisted extractions (UAE) are a novel and eco-friendly environmental technique as they can be incorporated with green solvents to recover the BCs from algae. The UAE technique is subject to non-chemical operation and non-toxic residue generation that is aligned with the green extraction processes.

F. Chemat et al. (2017) reported that the UAE process can produce low CO2 production with a proportion of 1:32:18 for UAE, soxhlet

extraction, and maceration. The other benefits of UAE are its low energy and retained thermally sensitive compounds [32]. The ultrasonic vibration includes two different cycles: compression and expansion, which can travel through the solid, liquid, and gas environment, resulting in the delocalization of molecules from their initial sites. The traveling of ultrasonic waves in a liquid medium can be employed for numerous applications, including extraction, modification, and cleaning. Nie et al., 2021 reported the UAE's usage in recovering fucoxanthin from brown algae Sargassum fusiforme using limonene and vegetable oils as solvents [33]. The optimal conditions of the UAE process were illustrated as follows: 40 mL/g LSR, 75 °C, and 53 % ultrasonic power for 27 min.

Ultrasonic bubbles generated from UAE are classified into two types: stable and transient bubbles. Transient bubbles are of concern because they generate sonochemistry in algae. Single bubble sonoluminescence possesses a long lifetime and the capability of luminescence and chemical reaction in an explosion. The size of these bubbles can be expanded by several compression and expansion cycles until they convert into an unstable form to produce smaller daughter bubbles. Eventually, these bubbles rupture to generate sonoluminescence and cavitation effect, producing high pressure and temperature in microenvironments. This effect is essential in enhancing the extraction efficiency of BCs from algae [7]. Fig. 1 presents the mechanism of UAE.

Ultrasonication generates negative pressure in the liquid medium, forming gas bubbles [34]. The implosion of gas bubbles creates the acoustic cavitation phenomenon, creating microjet, shock waves, and turbulent effects. These effects induce variation in algal tissues, including the fragmentation of algal cells, sonoporation, and the alteration of swelling capacity [34]. The shock waves are created by the radiation of pressure waves during the collapsing of cavitation bubbles. The difference in pressure field between the inside and outside of cavitation bubbles triggers the infiltration of liquid microjet during sonication [34]. These phenomena lead to the fragmentation of the cellular matrix, increasing the material's surface area and facilitating the dissolution of algal natural compounds. The erosion of algal surfaces is caused by the acoustic cavitation effect, which can trigger cellular damage. The turbulence effect of acoustic cavitation causes chaos in the liquid medium, which continuously refreshes the area around the algal surface, improving the mass transfer rate. These effects contribute to the enhancement of the extraction yield of BCs from algae [35,36].

The occurrence of salt, alcohol, sugar, and surfactant higher transient concentration triggers the delay in bubble coalescence, which happens because of attractive secondary Bjerknes forces. Coalescence can be accomplished after thinning and merging liquid films. However, the presence of solutes in the liquid raises solvents' surface tension, interfering with the large bubble formation. As a result, acoustic cavitation generates small active bubbles in the liquid system and limits the creation of larger inactive bubbles. Therefore, sonoluminescence amplitudes enhance with the rise of solutes at specific concentrations [7].

4.1.1. Ultrasonic power

The intensity of cavitation and erosion effect is varied based on the power of ultrasonic systems. However, the high intensity of ultrasonic power may not improve the extraction capacity as UAE yield is decided by other operational parameters such as BCs and algal species [37]. The ultrasonic amplitude, ranging from 20 to 900W, is popularly used for recovering BCs from algae [38]. Increasing ultrasonic power can generate larger bubble sizes and acoustic pressure, generating more serious collapse and chemical and physical effects. Although UAE's extraction efficiency increases with ultrasonic power enhancement, it might decrease with the excessive value of ultrasonic power. The enormous increase in ultrasonic power can cause the inter-collision of cavitation bubbles, which declining the destructive effect of cavitation bubbles, limiting the transfer of ultrasonic energy through a liquid medium, which reduces the extraction efficiency. The high temperature and free radical generation during the collapse of cavitation bubbles may trigger the thermal deterioration of natural compounds and declining extraction efficiency [38,39].

Olfat et al., 2024 employed NADES combined with UAE to recover BCs from *Hypnea flagelliformis* and investigated the enzyme-inhibitory activity of extracts [40]. The effect of variables, especially ultrasonic power from 220 to 440W, on the recovery yield of BCs was examined [40]. The increased ultrasonic power in the conditional ranges raised the extraction yield of phenolics, followed by remaining unchanged. The author reported the optimal conditions of NADES-based UAE at 80W ultrasonic power, 29.13 ml/g LSR, and 30 min extraction time to obtain the yield of phenolics at 88.31 mg/100 g. High-performance chromatography was used to determine six BCs in obtained extracts, including catechin gallate, epicatechin gallate, epigallocatechin gallate,

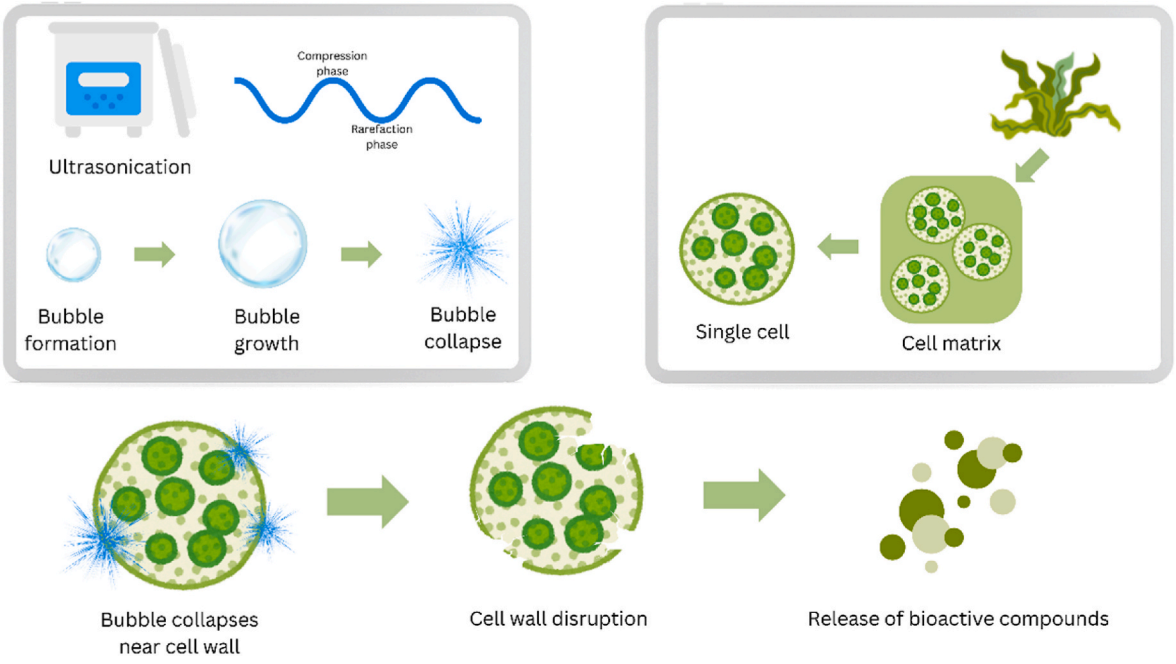

Fig. 1. The mechanism of cell wall destruction caused by the cavitation effect of acoustic vibration.

epicatechin, and gallic acid [40].

4.1.2. Ultrasonic frequencies

Ultrasonic frequencies ranging from 20 to 120 kHz are popularly employed to recover natural products from algae [37,38]. Low ultrasonic power and high frequency create numerous free radicals in extraction operations, whereas low-frequency and high ultrasonic power generate high mechanical and shear forces [38]. The diameter and lifetime of bubbles depend on the ultrasonic frequencies. The bubbles decrease with frequency increment, generating less power than the bigger bubbles. The high energy release of cavitation bubbles creates higher temperatures at molecular degrees and generates free radicals via vapor dissociation. The choice of low-frequency ultrasound stems from creating cavitation bubbles with larger sizes, creating the violent cavitation effect. This effect is reduced with frequency increments because of the formation of numerous bubbles with small diameters [38]. The frequency and the period of the rarefaction cycle negatively correlate. The high intensity is necessary at high ultrasonic frequencies to reach the desirable acoustic cavitation and reduce the cohesiveness between solvents and samples [32,37].

Krishnamoorthy et al., 2023 employed ultrasonic treatment to improve lipid acquisition from *Nannochloropsis Oculata* for producing biodiesel [41]. The author optimized the lipid extraction from microalgae using UAE with ultrasonic frequency and ultrasonic time. The optimal conditions of ultrasonic treatment were 80 kHz of frequency and 15 min of ultrasonic treatment time to acquire 17.9 % of lipid yield. This result contrasted with the previous study, in which high ultrasonic frequencies (>40 kHz) showed a greater effect on algal cells than low ultrasonic frequencies (<40 kHz) [38]. It can be attributed to the algal cells being easily disrupted by small cavitation bubbles. The higher frequency generated more cavitation bubbles than the lower frequency; thus, the destructive effect of cavitation on algal cell walls caused more damage at higher frequencies [38].

4.1.3. Ultrasonic pulsation

Ultrasound pulsation is a term in which the transducer is active and inactive. The effect of pulsation variation on the extraction efficiency of BCs from algae has been investigated. The UAE conducted in a pulsed mode declines the generation of cavitation bubble quantities. However, this mode increases the intensity of the collapsing cavitation bubble, triggering cellular matrix fragmentation and enhancing the yield of extraction processes [32]. Moreover, the pulse mode decreases energy usage for extraction processes and prevents overheating ultrasonic devices. The large gas bubbles formed through non-pulsed mode sonication can reduce the pressure difference between the inside and outside cavitation bubbles, reducing the intensity of acoustic cavitation. Pulsed sonication decreases the large gas bubble generation, enhances acoustic cavitation, and forms a more homogeneous acoustic field in the extraction medium [42].

Putra et al., 2022 employed UAE to extract phenolic compounds from red algae [28]. A Box-Behnken Design model (BBD) was employed to optimize the UAE process with five factors: ethanol concentration, temperature, pulse duty-cycle, LSR, and ultrasonic power. The optimal conditions of the UAE process were found: 100 % ultrasonic power, 1 s^{-1} of pulse duty-cycle, 52.5 °C, 50 % ethanol concentration, and 30 ml/g of LSR to get approximately 0.4-mg gallic acid equivalent (mg GAE)/g of dried samples. The pulse duty cycle positively affected the phenolic recovery yield, which affected the collapse pressure, generating higher local temperatures and a suitable extraction environment [28].

4.1.4. Ultrasonic time

Ultrasonic time significantly impacts the extraction efficiency of BCs from algae. Increasing ultrasonic time improves UAE process efficiency at the initial phase, followed by a decrease with the prolonged ultrasonic time [43]. The cavitation effect of ultrasound increased the hydration capacity of material, fragmentation, and microchannel generation in the cellular tissue of algae [44]. This effect fosters mass transfer rates and diffusion capacity of solvent into the algal matrix, improving the extraction yield of bioactive components. The continuous cavitation for the extensive extraction time deteriorates bioactive components. Furthermore, the prolonged ultrasonic time can affect the structure of bioactive components and cause a saturation effect, declining extraction yields [44].

Olfat et al., 2024 used NADES combined with UAE to recover BCs from *Hypnea flagelliformis* [40]. The author reported the optimal conditions of NADES-based UAE at 80W ultrasonic power, 29.13 ml/g LSR, and 30 min extraction time to obtain the yield of phenolics at 88.31 mg/100 g. The author showed that time had a significant effect on the recovery yield of natural components. The extraction process is divided into two main stages: washing and slow extraction. In the washing stage, the BCs on the outer layer of algal cells were solubilized and recovered by solvents, which was coupled with the rapid rise in extraction rate. In the slow extraction stages, the BCs in the inner layer of algal cells moved gradually into solvents by diffusion and osmotic phenomena. Based on the proposed mechanism, the adequacy of extraction time was necessary for solvent penetration into the algal matrix to recover BCs, improving the extraction yield [40].

4.1.5. Temperature

The temperature variation that affects the recovery yield of bioactive components from algae has been examined. The enhancement in temperature at a moderate level improves the recovery of BCs from algae. However, the excessively high temperature causes a reduction in the extraction yield of bioactive components from algae. The increasing UAE yield with the rise in temperature can be attributed to the improvement in the solubility and desorption capability of target analytes in solvents. Moreover, the high temperature reduces solvent viscosity and surface tension, boosting algal tissues' mass transfer and solvent diffusion capability. Nevertheless, continuously increasing temperature may improve the deterioration rates of bioactive components because of reducing cavitation effects [32,37].

Putra et al., 2022 employed UAE to extract phenolic compounds from red algae [28]. The optimal conditions of the UAE process were found: 100 % ultrasonic power, 1 s^{-1} of pulse duty-cycle, 52.5 °C, 50 % ethanol concentration, and 30 ml/g of LSR to get approximately 0.4 mg GAE/g of dried samples. The extraction yield of BCs increased when the temperature was 52.5 °C, followed by a decrease. The suitable temperature avoided the degrading of BCs and endorsed deteriorating the algal matrix, boosting solvent diffusivity and mass transfer [28].

4.1.6. Liquid-to-solid ratio (LSR)

Liquid-to-solid ratio is the volume of solvents (ml) per weight of materials (g). LSR is one of the important conditions during mass transfer because more solvent volumes promote the diffusion operation in the cellular matrix. The extraction efficiency of UAE is enhanced with rising LSR to a specific level, followed by a decline with the continuous increase of LSR. The cohesive forces of molecules in the extraction medium are loosened by the negative pressure of expansion cycles to form acoustic cavitation bubbles. Nevertheless, the low LSR cannot have a desirable cavitation effect due to the high viscosity. Furthermore, the concentration and viscosity of the extraction medium drop with the initial rise of LSR, strengthening the cavitation effect in an extraction medium. The higher distinction in concentrations boosts the diffusion capacity and solubility of the target analytes into a solvent, increasing the extraction yield. The deterioration of these compounds with a rising cavitation effect can be accounted for by the decrease in the extraction efficiency of BCs at excessive LSR [37,38,45].

Venansius G.P. Putra et al., 2022 employed UAE to extract phenolic compounds from red algae [28]. The optimal conditions of the UAE process were found: 100 % ultrasonic power, 1 s^{-1} of pulse duty-cycle, 52.5 °C, 50 % ethanol concentration, and 30 ml/g of LSR to get approximately 0.4 mg GAE/g of dried samples. The LSR positively

affected the extraction yield of BCs, which increased with the elevated LSR. The explanation for this phenomenon was aligned with the reason mentioned above [28].

4.2. Microwave

The mechanism of microwave-based heating is illustrated in Fig. 2. Microwave power is sent directly to algae via molecular interplays with electromagnetic fields [46]. Specifically, electromagnetic waves pass through algae, interact with polar molecules that receive energy, and change it to heat. This effect leads to a reduction in microwave field intensity with a rising distance from the algal surface. The two main mechanisms for the transformation of microwave power to heat in algae are ionic conduction and dipole rotation. Algae and green solvents possess ionic and dipolar molecules; thus, ionic conduction and dipolar rotation happen simultaneously, causing algae's instantaneous heating up [47]. When distilled water is employed as a solvent, dipole rotation acts as the primary mechanism. The ionic conduction plays a minor role in this extraction process because of the unrestricted ionic in algae solubilized in distilled water. When acid, alkaline, and salty solutions are employed as solvents, increasing the concentration of ionic substances improves the heating by ionic conduction [46]. Based on the rapid heating of the polar green solvents and algae, MAE considerably decreases extraction time in comparison to conventional methods which depend on slow external heating. Additionally, MAE minimizes the contact of algae with prolonged heat, which is essential for retaining the integrity of bioactive compounds. MAE also improves the solvent permeability, increasing the contact between solvents and target analytes within the algae matrix. So, MAE shows a higher extraction yield and ensures the stability of bioactive compounds in algae [48].

4.2.1. Liquid-to-solid ratios

Liquid-to-solid ratios are an important parameter for the MAE process because they directly affect the heating capacity of microwaves [49]. A suitable ratio of LSR ensures homogeneity and heating effectiveness. The low ratio of LSR resists mass transfer because the high density of BCs is distributed in limited regions, decreasing the BCs' motion out of algal cells [50]. The excessively high LSR triggers ineffective microwave heating since solvents absorb microwave radiation, and the higher microwave energy is applied in samples. The excessive microwave energy can cause over heating, destroying the BCs from algae [50]. Parva Safari et al., 2015 optimized the MAE conditions to acquire BCs from *Chaetomorpha* sp. employing the Central Composite Design model and investigated the antioxidant activities of these compounds. The phenolic content and reducing power were 1.09 and 0.12 mg tannic acid equivalent/g, respectively, at the optimal MAE conditions, which were 25 % ethanol concentration, 300W microwave power, and 8 min extraction time [29].

4.2.2. Microwave power and extraction temperature

In algal extraction, excessive microwave power may trigger low extraction efficiency because of the deterioration of thermal sensitive substances. The extraction efficiency improves with enhancing microwave power to limitation, followed by stability or decrease [50,51]. Microwave power induces localized heating in the algal cells and is a driving force for MAE to devastate the algal matrix. This effect promotes the diffusivity and solubility of analyte in the solvents, enhancing the extraction efficiency and shortening extraction time. The power level merely shows insufficient data on the absorption capacity of microwave energy in the extraction medium.

Alfaro et al., 2003 referred to energy density, which is power per mass for a fixed amount of time, to discover the influence of microwave power during MAE. They presented that when microwaves ruin material matrix, the natural products move from material to solvents. Excessive microwave power density limitedly contributed to the discovery of interplays between microwaves and extraction solvents within materials [52]. There is a positive correlation between microwave power and temperature. Rising temperature increases solvent power because of a decline in surface tension and viscosity [53]. High microwave power of MAE over the suitable power decreases extraction efficiency due to the thermal deterioration of BCs. Xiao et al., 2010 found that the extraction efficiency decreased when the temperature was over 110 °C because of the thermal instability of flavonoids at these temperatures. The choice of extraction temperature relies on the durability and extraction efficiency of target analytes. The regulation of temperature to ensure stability and reach high extraction efficiency for target analytes is essential for algal extraction [54].

4.2.3. Extraction time and cycles

In addition to microwave energy, extraction time and cycles are important factors significantly impacting the extraction yield of natural products from algae. Even at low energy, the prolonged microwave extraction time declines extraction efficiency because of the degrading chemical structure of natural compounds [49]. The MAE extraction time alters from several minutes to a half hour to avoid oxidation and thermal deterioration of BCs. The extraction time of MAE can be prolonged by up to an hour when extracting essential oil using solvent-free microwave-assisted extraction. However, when extensive extraction time is necessary for extracting BCs, the ability for thermal deterioration can be decreased via the extraction cycle. This phenomenon can be controlled

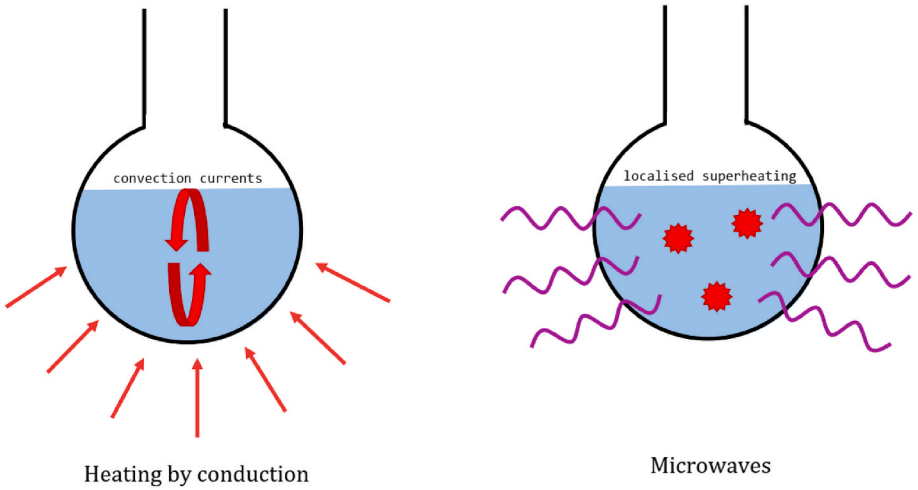

Fig. 2. The conventional heat transfer and the microwave-based heating.

by adding fresh solvent to extracted material and replicating the extraction procedure to ensure the accomplishment of extraction. The total figure for cycles is different from case to case. The division of long extraction time into cycles can save energy usage for MAE processes [53].

Lucía Cassani et al., 2011 extracted phenolics, flavonoids, and fucoxanthins from *Ascophyllum nodosum* using ethanol-based MAE. The author employed the Central Composite Design model to optimize the MAE processes and investigated the biological activity of obtained extracts at optimal conditions [55]. The optimal conditions of MAE were 10.4 bar and 46.8 % ethanol concentration for 3 min to obtain the phenolics, flavonoids, and fucoxanthins at 87.55, 15.72, and 2.55 mg/g dw, respectively. The research presented the significant effect of time on the extractability of natural components. The recovery yield of these compounds increased with the increment in extraction time, which can be explained by the reasons mentioned above.

4.3. Enzymatic

Enzyme-assisted extractions (EAE) have been used for extracting phytochemicals from algae and altered conventional extraction techniques due to their green, environmentally safe, and highly efficient properties. The algal cell walls are a mixture of cellular wall polysaccharides, such as cellulose, hemicellulose, sporopollenin, and algaenan [56]. Algal cell walls consist of two layers in which the external wall possesses polysaccharides like agar, pectin, algaenan, and alginate. The internal wall contains cellulose fibrils, hemicelluloses, pectins, soluble proteins, and fucans [57]. Various bioactive components occur in algal tissue, which conventional extraction cannot recover because of their linkages with polysaccharides and lignins.

Enzymatic pre-treatment increases the extraction yield of free BCs since this process breaks down the linkages between BCs and macromolecules [58]. Alpha amylase, cellulase, proteins, and pectinase are commonly employed for pre-treatment to improve the release of BCs from algae to solvents [58]. Various factors such as enzyme components, enzyme concentrations, solvents, liquid-to-solid ratios, pH, temperature, enzyme/substrate ratios, and time can affect the extraction efficiency of BCs from algae. These parameters impact the enzyme activity, which is responsible for the degradation of algal cell walls [58]. The drawback of enzymatic-assisted extraction is a high industrial-scale cost when treated with high enzyme-to-substrate ratios [36]. The extraction procedure and principle of MAE are shown in Fig. 3.

4.3.1. Enzyme concentration

Enzyme concentration influences the recovery yield of BCs by changing the algal cell wall-enzyme interaction. The enzymes connect with the algal cell wall, and the substrate linkages are degraded to form the smaller substances. Increasing enzyme concentration improves the reaction velocity until the equilibrium of substrates and products is formed. The recovery yield of BCs from algal cells is proportional to enzyme concentration within a specific range. The higher enzyme concentration increases the interaction between enzymes and substrates, enhancing algal cell deterioration and releasing BCs [59]. Nevertheless, when the enzyme concentration exceeds the specific values, the recovery yield of BCs stabilizes. This phenomenon may result from the substrate saturation effect, reducing the cell wall degradation of enzymes. Hoang Chinh Nguyen et al., 2024 employed EAE to acquire phenolics from *Padina gymnospora*. Alcalase showed the highest extraction yield of phenolics among three enzyme preparations (Cellulast, Pectinex, and Alcalase), and then the EAE process was optimized using the Central Composite Design model [60]. The optimal conditions of the MAE process were LSR of 61.31 mL/g, enzyme concentration of 0.32 %, and 60.5 °C for 1.95 h to obtain 97.6 % of the total phenolic content (TPC) of dried materials. The author reported that enzyme concentration significantly impacted the recovery of phenolics. The abovementioned reason can explain the improvement of phenolic recovery at high enzyme

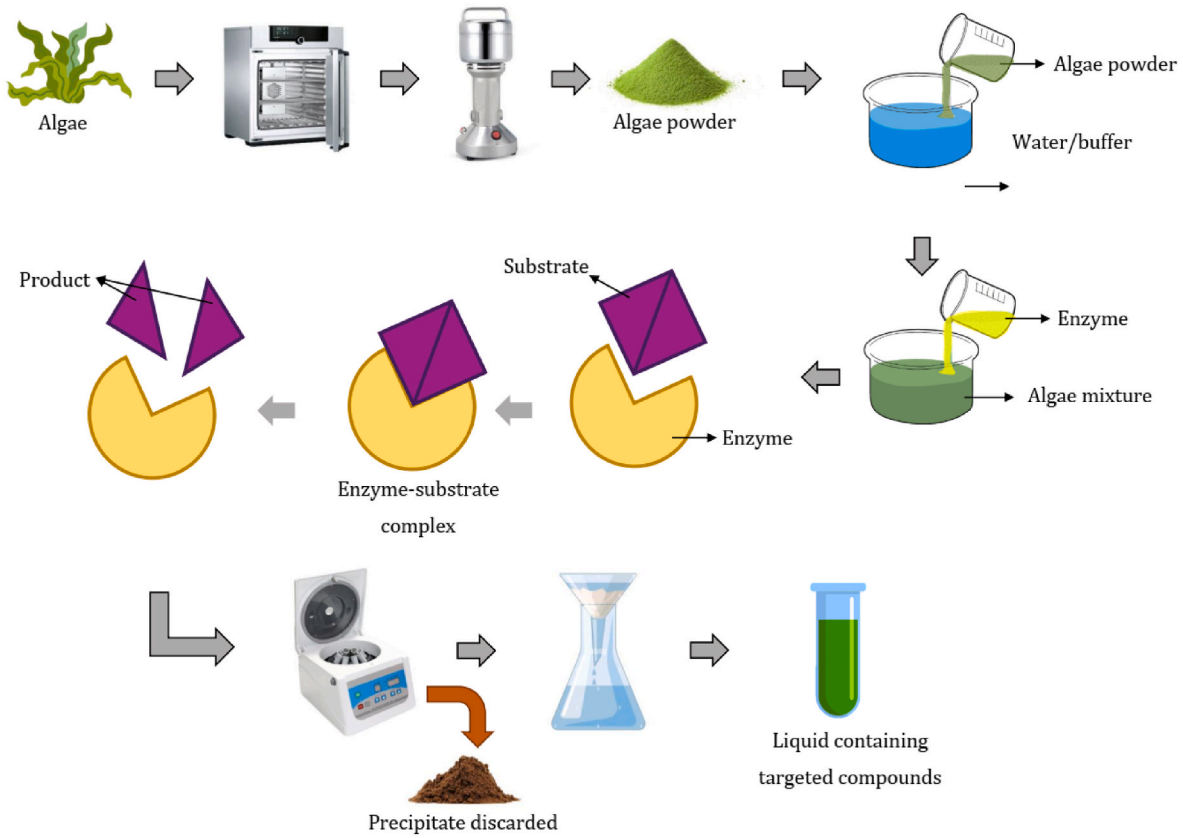

Fig. 3. The mechanism and procedure of enzymatic-assisted extraction to obtain BCs from algae.

concentrations. However, the low recovery yield of these compounds can be attributed to enzyme aggregation [60].

4.3.2. pH

The nature of enzymes is proteins whose configurations are significantly impacted by pH. This effect can vary the enzyme activity, influencing the extraction yield of BCs from algae [61]. EAE commonly uses phosphate buffer, hydrochloric acid, and sodium hydroxide to maintain pH stability at optimal values and ensure enzyme activity. When the optimal pH of the enzyme is in alkaline and acidic regions, the dissociation of hydroxyl groups in protein and the attack of hydronium ions to glycoside linkages occur. This effect can improve cell wall destruction, increasing BCs' recovery yield [62]. When the optimal pH values of enzymes are near the isoelectric point of proteins, the protein dissociation is decreased. This effect reduces the interaction between proteins and enzymes, interfering with the movement of BCs in the cytosol into solvents [63]. In practice, the enzyme preparation consists of different enzyme types employed in EAE to reach the highest degradation of cell walls.

E. Trigueros et al., 2021 employed EAE to recover phenolic compounds from the sugar-extracted red seaweed. The author reported that the mixture of various enzyme preparations, such as cellulase, protease, and xylanase, showed no higher extraction efficiency than cellulase. The optimal conditions of the EAE process were 8 % enzyme concentration and pH 5 to obtain the bound phenolic content at 7.5 mg GAE/g [64]. The research did not explain the effect of pH on the recovery yield of BCs. The improvement of extraction yield at low pH can be attributed to the destruction of vacuoles in algal cells [65]. Additionally, the trend of this research contrasted with the previous study, which can be ascribed to the difference in algal cell structure.

4.3.3. Temperature

Rising the extraction temperature can decrease the extraction mediums' overall viscosity and improve the BCs' diffusivity. The penetration and diffusion capacities improve with temperature increments until they peak at a maximal value. When the temperature exceeds the optimal activity values of enzymes, the enzyme configurations are changed. The variation in enzyme configuration reduces their activities, decreasing the hydrolysis capabilities and bioactive compound release [66]. Thus, a suitable temperature of EAE should be found to ensure the maintenance of enzyme activity and limit the thermal deterioration of BCs. A suitable temperature also assists in reducing the energy consumption of extraction processes while maintaining the high recovery yield of BCs.

S I Rahmawati et al., 2020 employed papain, which is a type of protease in papaya, to enhance the extraction of polyunsaturated fatty acids (PUFA) from *Caulerpa lentilifera*. The optimal conditions of the EAE process were 0.5 % of papain concentrations, 60 °C of extraction temperature, and 16h of incubation time [67]. The research also used gas chromatography-mass spectrometry to determine the fatty acid profile of extracts. The fatty acid composition of extracts was mainly omega six and omega nine fatty acids. However, the research did not explain the effect of extraction temperature on the recovery yield of fatty acid. From our perspective, the temperature might affect the enzymatic configuration, which is integral to enzyme activity. Excessively high temperatures can cause the irreversible denaturation of protein, which declines the enzymatic activities and extraction yield.

4.3.4. Liquid-to-solid ratios (LSR)

LSR impacts the bioactive compound release by affecting the enzyme-algae interaction. Water hydrates enzymes to conduct diffusion, migration, and hydrolysis. The viscosity of the extraction medium can be changed by adjusting LSR, which alters the degree of diffusion and movement of enzyme and algal cell walls. When LSR is low, the high viscosity of thick suspension limits the contact of enzymes with substrates, reducing the efficiency of algal cell wall degradation [68]. The higher LSR increases the contact between algal cells and enzymes, enhancing cell wall degradation and bioactive compound release [69]. The excessive LSR does not significantly affect the enzyme's function; however, it can increase the wastewater volume and the running cost. Emer Shannon and Nissreen Abu-Ghannam employed EAE to obtain fucoxanthin from seaweed. The optimal conditions of the EAE processes were 0.52 % of enzyme concentrations, 5.37 % of seaweed mass, and 3.05h of incubation time [65]. The author reported the effect of pH and type of enzyme on the recovery yield of fucoxanthin. However, the explanation for these effects, which is not elucidated, can be aligned with the abovementioned reason.

4.3.5. Time

The hydrolysis time depends on the algal cell walls' chemical composition, structure, and thickness. Extensive extraction time can improve the deterioration of algal cell walls, increasing the extraction yield of BCs. Nevertheless, the prolonged extraction time is unnecessary for manufacturing industries since it raises energy consumption and running costs [70]. Recently, the investigation of the effect of time using green-solvent-based EAE on the recovery of BCs from algae is limited. The review employed a study using non-algal biomass as an example. Tan Phat Vo et al., 2023 employed the NADES-based EAE process to extract BCs from spent tea leaves. The suitable conditions of the NADES-based EAE process were 40 ml/g of LSR, 15 U/g of enzyme concentration, and 60 min of incubation time. The improvement of recovery yield by incubation time could be explained by the fact that cellulase hydrolyzed the glycoside linkages in the cellulose of tea leaf cells at the beginning of the extraction process. This activity improved the movement of BCs in inner cells to solvent [71].

4.4. Supercritical fluid

Supercritical fluid extraction replaces traditional extraction techniques with improved transportation properties, promoting the movement of solvents into the algal matrix and fostering the extraction yield. Supercritical fluids have liquid and gas properties, and their polarity can be changeable by varying pressure and temperature. The benefits of the SFE process are that it has no organic solvents, high selectivity, and is safe, automated, and simple. On the other hand, the drawbacks of SFE are the high cost of equipment, low extraction efficiency of BCs with high and average polarity, and high power consumption [72]. The extractability of supercritical fluids (SF) depends on the considerable alteration in the solvating power of SF, which is reached via heating and pressurization. The mechanism of SFE is primarily constructed by various processes: mass transfer by convection and diffusion, phase equilibrium, and solvent removal through expansion. The high diffusion capacity and low viscosity enable the fluid to penetrate into an algal matrix as gas and solubilize the target analyte as liquid [73]. The effectiveness of SFE can be contingent on extraction time, flow velocity, co-solvents, pressure, and temperature. A graphic of solute contents as a function of time, co-solvents, or flow velocity to material mass ratios is commonly employed as a kinetic representation of SF from a solid matrix [74]. The kinetic extraction curves help scale up operations and calculate processing costs.

The overall occurrence of extraction procedures can be arranged in three stages according to mass transfer rules. Convective mass transfer is the primary mechanism in the first stage, which is the stage of constant extraction rate. The convection mechanism combines with the diffusion mechanism in the second stage, which is the falling extraction rate stage. The diffusion-controlled period is the stage where target analytes are removed. The main mechanism is the diffusion of the remaining analytes from the algal matrix to the CO_2 medium [75]. The extraction mechanism of SFE is presented in Fig. 4.

In terms of environmental implications, SFE is suitable for environment sustainability because of extraction processes employing carbon dioxide as a green solvent. CO2 can be generated through various

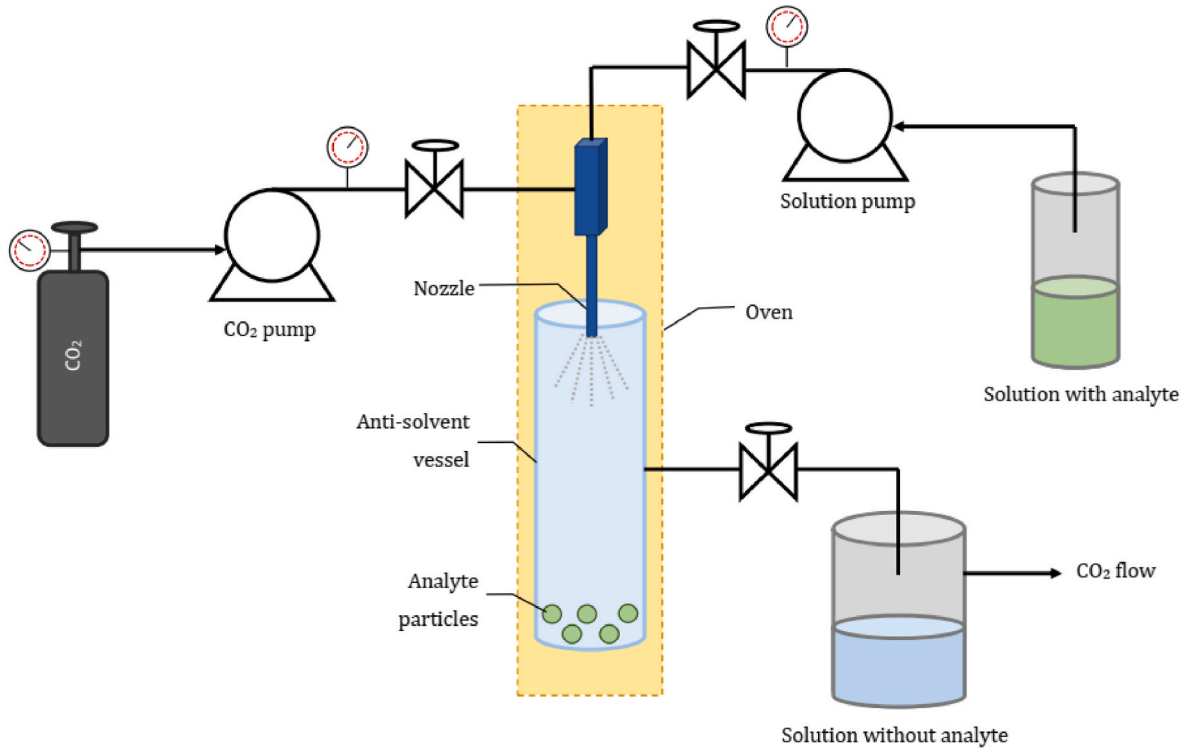

Fig. 4. The diagram for the supercritical extraction procedure to obtain BCs from algae.

biological processes, such as the conversion of lignocellulose waste, which can be used for the SFE process. The SFE process also reduces organic solvent usage, which decreases the effect of organic solvent toxicity on human health. SFE can provide the various characteristics of dense gases, including high compressibility and diffusivity. The high evaporation ability and the possibility of fine-tuning solvent power via modulating density are important in extracting bioactive compounds. SFE has various environmental benefits, including lower energy usage, the use of green solvents, the recycling of solvents, and non-additional purification steps. From these benefits, SFE has a greatly beneficial impact on the environment when the SFE process is scaled up for industrial applications. In terms of economic aspects, there are several factors that need to be considered before broadening the SFE process on the industrial scale. The challenges in SFE are the cost of retaining high-pressure conditions, controlling carbon dioxide recycling, and ensuring safety on a large scale. The cost of manufacturing (COM) should be considered, which consists of operating expenditures (OPEX), capital expenditure (CAPEX), and life cycle costs (LCC). The manufacturer also considers the use of raw materials and solvents, which are the primary factors in raising production costs. Raw materials have high differences in the components of natural compounds from algae because of seasonal variation and soil conditions. Additionally, its availability is restricted because of the productivity and transport of the region [76].

4.4.1. *Pressure*

Pressure plays an important role in SFE because it retains the liquid form of water above the boiling point. The pressure generates a destructive effect on the algal matrix. Supercritical water is weakly contingent on pressure; thus, increasing pressure shows a minor effect on extraction efficiency [77]. However, the considerably increased pressure can support the movement of solutes from the sample pores to solvents [78]. Cvetanović et al., 2017 founds the optimal conditions of apigenin using subcritical water as a solvent at 30 ml/g LSR, 3 Hz agitation rate, 45 bar, and 115 °C for 30 min. Cvetanović et al., 2017 reported that the total phenolic contents increased from 90 to over 100 % when the pressure rose from 10 to 45 bar [78].

4.4.2. *Temperature*

Temperature alters the physiochemical properties of water, such as viscosity and surface tension. The increment in extraction temperature declines in surface tension and viscosity, which decreases the force of hydrogen bonds and intermolecular interaction between solutes and solvents [79]. These alterations change the dielectric constant of water close to ethanol and methanol, improving the solute solubility in water [79]. Additionally, these changes boost the mass transfer rate and solubilize various BCs with different polarities. Previous studies reported that the excessively increasing temperature triggers a drop in solute concentration due to BCs' thermal degradation and molecular transformation [80]. Determining the optimal extraction temperature in SFE for different target analytes in algae is necessary. Mari Carmen Ruiz-Domínguez et al., 2022 employed SFE to extract fucoxanthin from *Phaeodactylum tricornutum* before they applied SFE extracts to biogass production [81]. The optimal conditions of the SFE process were 30 °C, 30 MPa, and 40 % ethanol concentration to acquire the fucoxanthin content at 85.03 mg/g. The author reported that the higher purity of fucoxanthin was obtained at low temperatures.

4.4.3. *Co-solvent*

The supercritical fluids have low polarity, so they cannot extract the high-polar BCs. Adding a low amount of polar co-solvents, such as alcohol, is necessary to enhance the polarity and extraction performance [82]. The presence of co-solvent enhances the accessibility of BCs in SF through decreasing fluid viscosity [83]. Additionally, co-solvents improve the molecular affinity between target analytes and solvents by boosting the mass transfer rate while raising the polarity of SF. The synergy of phenomena substantially increases the overall extraction performance [84]. The pH and co-solvents concentration influence the extraction yield and target analyte purity. However, the reports that presented these influences have not been published. Mari Carmen Ruiz-Domínguez et al., 2017 employed SFE to extract fucoxanthin from *Phaeodactylum tricornutum* before they applied SFE extracts to biogass production [81]. The optimal conditions of the SFE process were 30 MPa, 30 °C, and 40 % ethanol to acquire the fucoxanthin content at

85.03 mg/g. However, the author did not report the explanation for the significant increase in fucoxanthin at 30 % ethanol concentration and the decreasing trend over 30 % ethanol concentration. The enhancement in the recovery yield may attributed to the adjustment of solvent mixture polarity close to fucoxanthin polarity [84].

4.4.4. Time

The extraction time is one of the important parameters in SFE due to its influence on the running cost, extraction efficiency, and durability of BCs [85]. The rapid solubility of crocin happens at the initial stage of SFE, followed by a decline with the prolonged extraction time. These results are contingent on other parameters such as extraction time, extraction temperature, co-solvents, and the natural properties of target analytes and algae [86]. It can be explained that the SFE process reaches the equilibrium or degrades the extracted components. The latter reason is commonly due to the thermal instability of bioactive components at high temperatures. Therefore, the extraction yield of these compounds declines with the extensive extraction time [86]. The optimal extraction time should be determined to ensure the overall production cost. Aleksandra Cvetanović et al., 2017 isolated apigenin from chamomile using subcritical water as a solvent. The optimal conditions of the subcritical water extraction process were LSR of 1:30 ml/g, agitation rate of 3 Hz, 45 bar, and 115 °C for 30 min [78].

4.4.5. Liquid-to-solid ratio

The liquid-to-solid ratio influences the dissolution capability and equilibrium of the SFE process [87]. A rise in the liquid-to-solid ratio improves the target analytes' concentration gradient, enabling a higher extraction rate [78]. Specific parameters such as extraction time and running costs should be considered when investigating optimal liquid-to-solid ratios. An optimal liquid-to-solid ratio ensures the appropriate gradient between the algal matrix and solvents during extraction. Cvetanović et al., 2017 founds the optimal conditions of apigenin using subcritical water as a solvent at 30 ml/g LSR, 3 Hz agitation rate, 45 bar, and 115 °C for 30 min [78].

4.4.6. Flowrate

SFE commonly occurs in a stationary operation. For the continuous SFE process, the flowrate beneficially affects the extraction yield of target analytes by moving the equilibrium and enabling better solvent flux through the algal matrix. This effect boosts the extraction rate and reduces the retention time of target analytes in the solvent. The effect of

Table 1
The research of green solvent-based ultrasonic-assisted extraction to recover BCs from algae.

Materials	Substances	Solvents	ETE	Extraction conditions	EEF	References
Chromochloris zofingiensis	Canthaxanthin	Deep eutectic solvents	UAE	• Temperature: 50 °C • Time: 49 min • The molar ratios of octanoic acid and decanoic acid: 2.3:1 • Solid-to-liquid-ratio: 66.2 mg/ml	60.5 μg/mL	[89]
Undaria pinnatifida	Fucoxanthin	Ethanol	UAE	• Ultrasonic amplitude: 36 % • Time: 31 min; time: 55 °C • Liquid-to-solid ratio (LSR): 40 ml/g	1.56 mg/g of dried materials	[91]
Arctic Fucus vesiculosus	Phlorotannins	Natural deep eutectic solvent	UAE	• Lactic acid: choline chlorides: 3:1 • Time: 23 min; water content: 30 % • Liquid-to-solid ratios: 12:1	137.3 mg/g of dried materials	[90]
Porphyra haitanensis	Phenolics	Ethanol	UAE	• LSR: 31 ml/g • Ethanol concentration: 56.84 % • Time: 25 min • Temperature: 50.25 °C	6.88 mg galic acid equivalent (GAE)/g of dried material	[92]
Sargassum aquifolium	Phenolics	Ethanol	UAE	• Time: 30 min • Ethanol concentration: 96 % • LSR: 10 ml/g • Temperature: 25 °C	52 mg GAE/g of dried material	[93]
Fucus vesiculosus	Phlorotannins	Ethanol	UAE	• LSR: 10 ml/g • Ethanol concentration: 50 % • Frequency: 130 kHz • Time: 30 min	57.11 mg GAE/g of dried material	[94]
Sargassum fusiforme	Fucoxanthin	Ethyl lactate	UAE	• LSR: 40 ml/g • Time: 27 min • Temperature: 75 °C • Amplitude: 53 %	696.85 μg/g of dried material	[33]
Hypnea flagelliformis	Phenolics	Deep eutectic solvents	UAE	• Choline chloride: lactic acid: 1:2 of molar ratio • 20 % of water content • LSR: 29.12 ml/g • Ultrasonic power: 80 % • Time: 30 min	87.98 mg/100 g of dried material	[40]
Spirulina platensis	Bioactive pigments	Natural deep eutectic solvent	UAE	• Glucose/glycerol/water: 1:2:4 of molar ratio • Time: 30 min • LSR: 20 ml/g	Phycocyanin: 3.79 mg/g of dried material; chlorophylls: 0.24 mg/g of dried material; carotenoid: 0.13 mg/g of dried material	[95]
Sargassum muticum	Phenolic compounds	Eutectic solvents	UAE	• Proline: propylene glycol: 1:4 of the molar ratio • 30 % of water content • Temperature: 60 °C • Time: 9 min	Salicylic acid: 26 μg/g	[96]

Note: ETE: extraction techniques; EEF: extraction efficiency.

flow rate is managed by the phase in which SFE kinetics is equilibrium. Thus, relying on the operating conditional range, the prolonged time can negatively affect the effectiveness of the flow rate on the extraction yield of target analytes. The drawback of an excessively high flow rate is to dilute extracts; thus, the concentration process after extraction is necessary. The additional step can increase the running costs of extraction processes; therefore, it is necessary to consider the additional cost when determining the best flow rate. De Melo et al., 2020 employed the SFE to extract omega-3 fatty acids from *Aurantiochytrium* sp. The author reported that the optimal conditions of the SFE process were CO2 flowrate: 12 g/min, 40 °C, and 30 Mpa for 360 min [88].

5. Application of green solvents with novel extraction techniques

5.1. Ultrasonic-assisted extraction

UAE is the intensification technique, which facilitates the movement of solutes into solvents. UAE is also a green, sustainable, cost-effective, and eco-friendly method, making this technique the potential alternative in large-scale industrial extraction. Several authors report the recovery of BCs from algae; detailed information on these works is presented in Table 1. Dan Yang et al., 2023 employed deep eutectic solvents (DES) coupled with UAE to recover canthaxanthin from *Chromochloris zofingiensis*. The author showed the superior extraction yield of DES-based UAE to ethanol-based one. The optimal extraction parameters of the DES-based UAE process were 50 °C, 49 min, the molar ratios of octanoic acid and decanoic acid: 2.3:1 and LSR 66.2 ml/g to acquire the canthaxanthin content at 70.4 μg/mL. The high extraction efficiency of DES-based UAE can result from the complete deterioration of algal cell walls. It can be attributed to the severe erosion and great penetration by DES and the mechanical vibration of ultrasonic waves, which foster the release of canthaxanthin from the algal matrix to solvent [89].

Ekaterina D. Obluchinskaya et al., 2023 reported the optimization of the NADES-based UAE process to recover phlorotannins from *Arctic Fucus vesiculosus*. In addition to optimization, the study also investigated the detailed profile of phlorotannins using tandem high-resolution mass spectrometry (HRMS). This research demonstrated that time, the water content in NADES, LSR, and the interaction between time and LSR significantly affected the extraction yield of phlorotannins from *Arctic Fucus vesiculosus*. LSR and water content directly influenced the overall viscosity of the extraction medium, in which high LSR and water content decreased that of the extraction medium. The low viscosity favored the contact between algae and NADES, which improved the concentration gradient within the algal matrix and efficient extraction. The optimal parameter of the NADES-based UAE process was lactic acid: choline chlorides: 3:1; time: 23 min; water content: 30 %; liquid-to-solid ratios: 12:1 to reach the phloratannin concentration at 137 mg/g of dried materials. The phlorotannins of *Arctic Fucus vesiculosus* consisted of various degrees of polymer from trimer to nonamer, which was detected by HRMS techniques. Thirty-two phlorotannins were identified in the extracts, including fucophlorethol, fucodiphlorethol, fucodiphlorethol, trifucophlorethol, trifucophlorethol, fucotriphlorethol, hexafucol, fucotetraphlorethol, heptafucol, fucophlorethol, octafucol, and nonafucol [90].

Jinggui Nie et al. investigated the optimal parameters of the UAE process to extract fucoxanthin from *Sargassum fusiforme* and established the kinetic models for this extraction process. From the polynomial regression model, the variables time, temperature, amplitude, and the interaction of time and amplitude significantly impacted the extraction yield of fucoxanthin from *Sargassum fusiforme*. The increased amplitude boosted the effect of acoustic cavitation, which enhanced the degradation of algal cell walls. The adequate extraction time generated a high slope of fucoxanthin concentration gradients between the algal matrix and the solvents, facilitating the release of fucoxanthin from cells to solvents and improving the extraction yield. However, excessive time and amplitude can decrease fucoxanthin yield due to fucoxanthin's destruction. This research also built the kinetic extraction of the UAE process. The optimal parameter of the UAE process was 40 ml/g of LSR, 75 °C, and 53 % amplitude of ultrasonic power for 27 min to obtain the fucoxanthin content at 696.85 μg/g of dried material. The kinetic models demonstrated that the initial extraction rate of fucoxanthin was decided by temperature. The second-order extraction rate constant (k) increased with the temperature in the range from 65 to 75 °C, followed by a decrease. The decrease in k value presented the deterioration of fucoxanthin [33].

5.2. Microwave-assisted extraction

The potentiality of MAE to obtain bioactive components from algae was investigated by scientists, and these reports are presented in Table 2. Bárbara C. Jesus et al. recovered salicylic acid from *Sargassum muticum* using eutectic solvents and MAE as the intensification technique. The proline: propylene glycol system showed the highest extraction yield of salicylic acid based on high-performance liquid chromatography (HPLC) results. The optimal MAE conditions were 30 % water content in NADES and 60 °C for 6 min to obtain the salicylic content at 26.69 ppm. Temperature and water content mainly affected the viscosity of solvents, which was an important mass transfer influencer. The adequacy of temperature and water content could reduce the viscosity of deep eutectic solvents, which fostered the mass transfer of salicylic acid from the algal matrix to solvents. However, excessive water content and temperature can destroy the hydrogen bond networks of solvents and phenolic compounds, causing a decline in extraction yield. Using the intensification technique as MAE for the short extraction time showed an equal extraction yield to maceration technique usage for the long extraction time. This result demonstrated that the employment of intensification techniques is more energy efficient, green, and sustainable than maceration [96].

Marco Garcia-Vaquero et al., 2018 employed MAE as the intensification technique to acquire phenolic compounds from *Fucus vesiculosus*. The optimal conditions of the MAE process were microwave power: 250W, time: 10 min, LSR: 10 ml/g, and 50 % of ethanol concentration to obtain phenolic, phlorotannin, flavonoid, tannin, and sugar contents at 391.2 mg GAE/g of dried material, 318.9 mg phloroglucinol equivalents/g of dried material, 202.6 mg quercitin equivalents/g of dried material, 161.0 mg catechin equivalents/g of dried material; and 199.9 mg glucose equivalents/g of dried material, respectively. The report also investigated the antioxidant activities of *Fucus vesiculosus* extracts obtained by novel extraction techniques. The antioxidant activities of these extracts were higher than those acquired by maceration. The higher antioxidant activity could be attributed to the high phenolic content obtained by novel extraction techniques [97].

Camille Juin et al., 2015 employed MAE to extract phycoerythrin, which is the important substance linking the core of phycobiliproteins to thylakoid membranes, from *Porphyridium purpureum* using water as a solvent. The optimal conditions of MAE were 40 °C for 10s to obtain the phycoerythrin extraction yield of 73.7 ± 2.3 μg/mg. MAE showed 1.08- and 3.8 times higher extraction yield and pigment purity than the soaking extraction technique. The devastating effects of MAE on algal cell walls were demonstrated by scanning electron microscopy. After microwave treatment, *Porphyridium purpureum* thylakoid membranes were significantly degraded by the high pressure and sudden water evaporation at local regions, resulting from the microwave's rapid heating effect. This destruction promoted the release of phycoerythrin into water, deeply buried in a thick exopolysaccharidic algal cell wall [98].

5.3. Enzymatic-assisted extraction

Enzymatic-assisted extraction is the intensification technique, improving the release yield of BCs. The cell wall of algae is commonly

Table 2
The research of green solvent-based microwave-assisted extraction to recovery BCs from algae.

Materials	Substances	Solvents	ETE	Extraction conditions	EEF	References
Ascophyllum nodosum	Polyphenol and β-carotene	Ethanol	MAE	• Time: 3 min • Ethanol concentration: 46.8 %	Polyphenols: 86.45 mg GAE/g of dried material; β-carotene: 0.05 μmol betacarotene/g of dried material	[55]
Sargassum muticum	Phenolic compounds	Eutectic solvents	MAE	• Proline: propylene glycol: 1:4 of the molar ratio • 30 % of water content • Temperature: 100 °C • Time: 6 min	Salicylic acid: 26.69 ppm	[96]
Kappaphycus alvarezii	Phenolic compounds	Ethanol	MAE	• LSR: 30 ml/g • Temperature 60 °C • Time: 15 min	5.57 mg GAE/g of dried materials	[99]
Phaeodactylum tricornutum	Phenolic compounds and carotenoids	Water and ethanol	MAE	• Ethanol concentration: 100 % • Time: 2 min • Temperature: 30 °C	Phenolics: 30.5 mg GAE/g of dried materials; carotenoids: 24.79 μg/g of dried materials	[100]
Undaria pinnatifida	Fucoxanthin	Ethanol	MAE	• Time: 3 min • Ethanol concentration: 100 % • Pressure: 2 bar	58.83 mg/g of dried materials	[101]
Fucus vesiculosus	Phenolic	Ethanol	MAE	• Microwave power: 250W • Time: 10 min • LSR: 10 ml/g • Ethanol concentration: 50 %	391 mg GAE/g of dried material	[102]
Sargassum vestitum	Phenolic compounds	Ethanol	MAE	• Ethanol concentration: 70 % • Time: 1.25 min • Power: 80 %	61.13 mg GAE/g of dried material	[97]
Porphyridium purpureum	Phycoerythrin	Water	MAE	• LSR: 350 ml/g • Temperature: 40 °C • Time: 10 s	73.7 ± 2.3 μg/mg	[98]

Note: ETE: extraction techniques; EEF: extraction efficiency.

structured by cellulose, alginate, and hemicellulose, which can be deteriorated by the enzyme hydrolysis [65]. Enzymatic-assisted extraction is a green technique because it conforms to the green chemistry rules. Recovering the BCs from algae was investigated by several researchers, and the reports are presented in Table 3. Xiaoyan Zhao et al., 2019 employed cellulase and pectinase to facilitate the acquisition of astaxanthin from *Haematococcus pluvialis*. The suitable parameter of the EAE was the mixture of cellulose and pectinase: 1.9:1 of volume ratios, pH: 5, temperature: 40 °C and incubation time: 1h to reach 60.93 % of the total astaxanthin contents in *Haematococcus pluvialis*. The pH affected the enzyme's stability due to the protein conformation variation. The pH exceeded the optimal range, which caused protein denaturation, reduced cellulase and pectinase activity, and decreased astaxanthin release. The concentration of cellulase and pectinase significantly impacted the release yield of astraxanthin from *Haematococcus pluvialis*. The increase in enzyme concentration at the specific range increased astaxanthin's release, which can be associated with the increment in the number of enzyme-substrate complexes. This complex played a crucial role in increasing the reaction rate because it enhanced the polymer conversion rate to smaller molecules. This effect increased the degradation of the algal cell wall. However, the excessive enzyme concentration decreased the astaxanthin concentration due to its degradation by long exposure to oxygen in the atmosphere [103].

Emer Shannon and Nissreen Abu-Ghannam 2018 employed Viszyme to extract fucoxanthin from *Fucus vesiculosus*. The optimal parameters of EAE were the 2:1 water-to-enzyme ratio, pH 4.5, and 5.4 %

Table 3
The research of green solvent-based enzymatic-assisted extraction to recovery BCs from algae.

Materials	Substances	Enzymes	ETE	Extraction conditions	EEF	References
Haematococcus pluvialis	Astaxanthin	Cellulase and Pectinase	EAE	• The mixture of cellulose and pectinase: 1.9:1 of volume ratios • Temperature: 40 °C • Incubation time: 1h	60.93 %	[103]
Sargassum dupplicatum	Phlorotannin	Cellulase, Termamyl, and Viscozyme	EAE	• Cellulase dosage: 7.5 % v/v • Incubation time: 3h • Temperature: 25 °C	4.45 mg/g of dried material	[105]
Ulva sp.	Ulvan	Protamex	EAE	• Enzyme concentration: 6 % v/v • Temperature: 50 °C • Incubation time: 3h	5.84 % of dried material	[106]
Fucus vesiculosus	Fucoxanthin	Viscozyme	EAE	• Water-to-enzyme ratios: 2:1 • Incubation time: 3.05h • Temperature: 40 °C • Enzyme solution-to-material: 1:5.37 ml/g	0.657 mg/g of dried material	[65]
Sargassum angustifolium	Phenolics	Viscozyme	EAE	• Incubation time: 20h • Temperature: 50 °C • Enzyme solution-to-material: 1:100 ml/g	8.25 mg GAE/g of dried materials	[104]
Sargassum boveanum	Phenolics	AMG 300L	EAE	• Incubation time: 20h • Temperature: 60 °C • Enzyme solution-to-material: 1:100 ml/g	7.48 mg GAE/g of dried materials	[104]

Note: ETE: extraction techniques; EEF: extraction efficiency.

algae-to-water ratios for 3.05 h of extraction time to reach the fucoxanthin content at 0.66 mg/g of dried material. Viscozyme is a commercial preparation composed of cellulase, beta-glucanase, hemicellulase, arabanase, and xylanase. The mixture of enzymes could break down various types of β-glycosidic linkages, significantly degrading *Fucus vesiculosus* cell walls and improving the release of fucoxanthin. In addition to enzymatic hydrolysis, the acidified water deteriorated algal vacuoles, increasingly releasing cell-linked compounds. The researchers also employed HPLC coupled with mass spectrometry to determine fucoxanthin content [65].

Sabeena Farvin K. Habeebullah et al., 2020 used commercial enzyme preparation (Flavourzyme) to extract BCs from *Sargassum angustifolium*. The optimal parameters of the EAE process were incubation time: 20h; temperature: 50 °C; and enzyme solution-to-material: 1:100 ml/g to acquire 8.25 mg GAE/g of dried materials. Using Flavourzyme also increased the antibacterial activities of enzymatic-assisted-based extracts. Flavourzyme encompassed endoprotease and exopeptidase, which can partially hydrolyze protein to generate peptides. These peptides can possess antibacterial activities, boosting extracts' general antibacterial activity [104].

5.4. Supercritical-fluid extraction

SFE is a replacer for the traditional extraction techniques with improved transport properties, fostering a rapid movement of solvent into an algal matrix and extraction rate. Carbon dioxide is the most popular solvent in the SFE technique due to its safety, greenness, sustainability, and non-flammability. Carbon dioxide possesses low surface tension, low viscosity, easy removal, and high diffusivity [107]. The reports related to applying the SFE technique in recovering BCs from algae are shown in Table 4. Myroslav Sprynskyy et al., 2022 reported the isolation of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) from *Pseudostaurosira trainorii* using the SFE technique. The suitable parameters of the SFE process were CO2 flowrate: 10 ml/min, temperature: 60 °C, pressure: 30 Mpa, and ethanol concentration: 10 % for 40 min to get the EPA and DHA contents at 33.7 and 0.5 mg/g of dried material [108]. MMR de Melo et al., 2020 employed supercritical carbon dioxides to recover phenolics and omega-3 fatty acids from *Aurantiochytrium* sp. The optimal parameters of the SFE operation for DHA were 300 bar, 80 °C and 6 gCO_2/min to obtain the DHA contents at 39.2 % of extracts, while that of phenolics were 200 bar, 80 °C and 12 gCO_2/min to obtain the phenolic contents at 2.24 mg GAE/g of extracts. An increase in pressure can improve the affinity of solvents with DHA molecules, increasing the extraction yield of DHA. However, an increase in temperature can promote the solubility of non-DHA substances, which reduces the extraction yield of DHA. Regarding phenolic compounds, temperature significantly contributed to the high extraction yield of phenolics, probably due to the temperature-based variation of solvent polarity close to phenolic polarity [88].

5.5. Comparison of extraction techniques using meta-analysis

The metadata analysis was conducted to compare the extraction yield of phenolic acquired from plants and algae employing UAE. MAE, EAE, and SFE. The metadata analysis result is illustrated in Fig. 5. The phenolic content of algae was obtained using green solvent-based UAE, MAE, EAE, and SFE, similar to that of plants. Additionally, among the four extraction techniques, MAE showed the highest yield of phenolic compounds. The highest extraction yield of MAE can result from two main reasons: the microwave-based heating effect and solvent polarity.

Table 4
The research of green solvent-based supercritical and subcritical fluid extraction to recover BCs from algae.

Materials	Substances	Solvents	ETE	Extraction conditions	EEF	References
Pseudostautosira trainorii	EPA, DHA	Supercritical CO2	SFE	• CO2 flowrate: 10 ml/min • Time: 40 min • Temperature: 60 °C • Pressure: 30 Mpa; and ethanol concentration: 10 %	EPA: 33.701 mg/g of dried materials; DHA: 0.455 mg/g of dried materials	[108]
Nannochloropsis sp.	EPA	Supercritical CO2	SFE	• CO2 flowrate: 8 g/min; time: 40 min • Temperature: 60 °C • Pressure: 30 Mpa • Ethanol concentration: 10 %	70.3 % of the total extracted saponifiable lipids	[109]
Aurantiochytrium sp.	Omega-3 fatty acids and Phenolic compounds	Supercritical CO2	SFE	• For fatty acids: o CO2 flowrate: 12 g/min o Time 360 min o Temperature: 40 °C o Pressure: 30 Mpa. • For phenolics: o CO2 flowrate: 12 g/min oTime: 360 min oTemperature: 80 °C o Pressure: 20 Mpa	Fatty acid: 39.2 % of extracts; Phenolic: 2.24 mg GAE/g of extracts	[88]
Phaeodactylum tricornutum	Fucoxanthin	Supercritical CO2	SFE	• LSR: 108.6 ml/g • Time: 60min • Temperature: 30 °C • Pressure: 30 Mpa • Ethanol concentration: 30 %	85.03mg/g of dried materials	[81]
Schizochytrium sp.	DHA	Supercritical CO2	SFE	• LSR: 108.6 ml/g • Time: 30min • Temperature: 76 °C • Pressure: 47 Mpa • Ethanol concentration: 1.25 ml/min	7.98 g of DHA/100 g of dried material	[110]
Monoraphidium sp	Astaxanthin	Supercritical CO2	SFE	• Temperature: 60 °C • Pressure: 20 Mpa	Astaxanthin: 2.02 mg/g of dried materials	[111]
Chlorella Vulgaris	Phenolic	Subcritical water	SFE	• Temperature: 100–200 °C • Pressure: 10.3 Mpa • Time: 20	58 % of the total phenolic contents of dried materials	[112]

Note: ETE: extraction techniques; EEF: extraction efficiency.

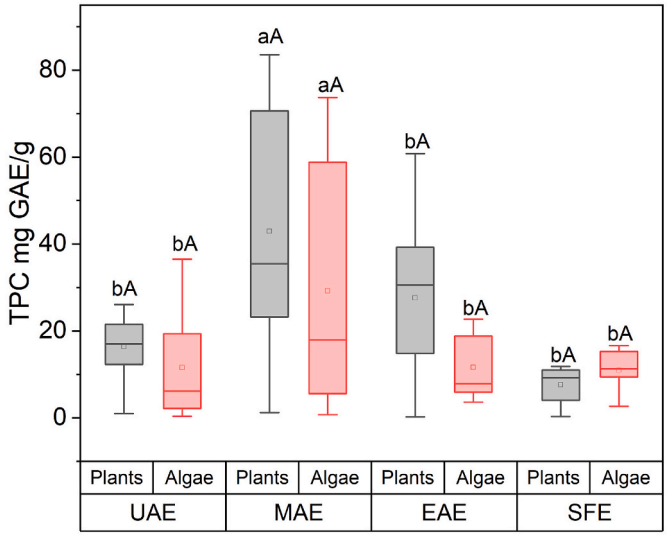

Fig. 5. Comparing the phenolic extraction yield obtained from plants and algae using UAE, MAE, EAE, and SFE. Different letters (a, b, A, and B) indicate the significance of statistical distinctions.

Two effects significantly improved mass transfer and encouraged the formation of microchannels on the surface of materials. However, the low solvent polarity can reduce the effect of microwaves on materials. The lower extraction yield of EAE, UAE, and SFE in comparison with MAE can be explained by the following reasons. The disadvantages of EAE and SFE in comparison with MAE are low mass transfer and long extraction time. Although UAE can generate microturbulence and the formation of microchannels on cell walls via the cavitation effect, the power of the cavitation effect can be reduced with material with significantly small particle sizes and rigid cell walls. To solve these problems, MAE can act as a pretreatment process or be simultaneously used with other extraction techniques. The cell wall disruption of MAE can facilitate the attachment of enzymes on cellulose chains during EAE, as well as the penetration of supercritical solvents during the SFE process. The phenomenon can improve the extraction yield of BCs.

6. Challenges and future perspectives

Future research should concentrate on the simultaneous and multi-stage processes of recovering BCs from algae, in which MAE acts as the pretreatment method (Fig. 6).

- The quantification of solvent dielectric constants should be conducted. Experiments are needed to quantify the heating level during the MAE process and how this impacts mass transfer and structural variation. Anna Rybinska-Fryca et al., 2018 employed the quantitative structure-property relationship (QSPR) method to predict the dielectric constant of ionic liquids, such as imidazolium, pyridinium pyrrolidinium, ammonium, and sulfonium. The research used three factors, namely the proportion of hydrogen atoms, the appearance-disappearance of C-O at topological length, and the coefficient sum of the last eigenvector from the Burden matrix calculated by the level of Van der Waals force to anticipate the dielectric constant of known ionic liquid. The dielectric constant of phosphorium, pyrrolidinium, and pyridinium was from 10 to 20, which was lower than ammonium from 50 to 70 (nearly water). Then, the 3D- QSPR was established to describe the molecular structure and predict the dielectric constant of new ionic liquid [113]. Therefore, 3D-QSPR can be used to predict

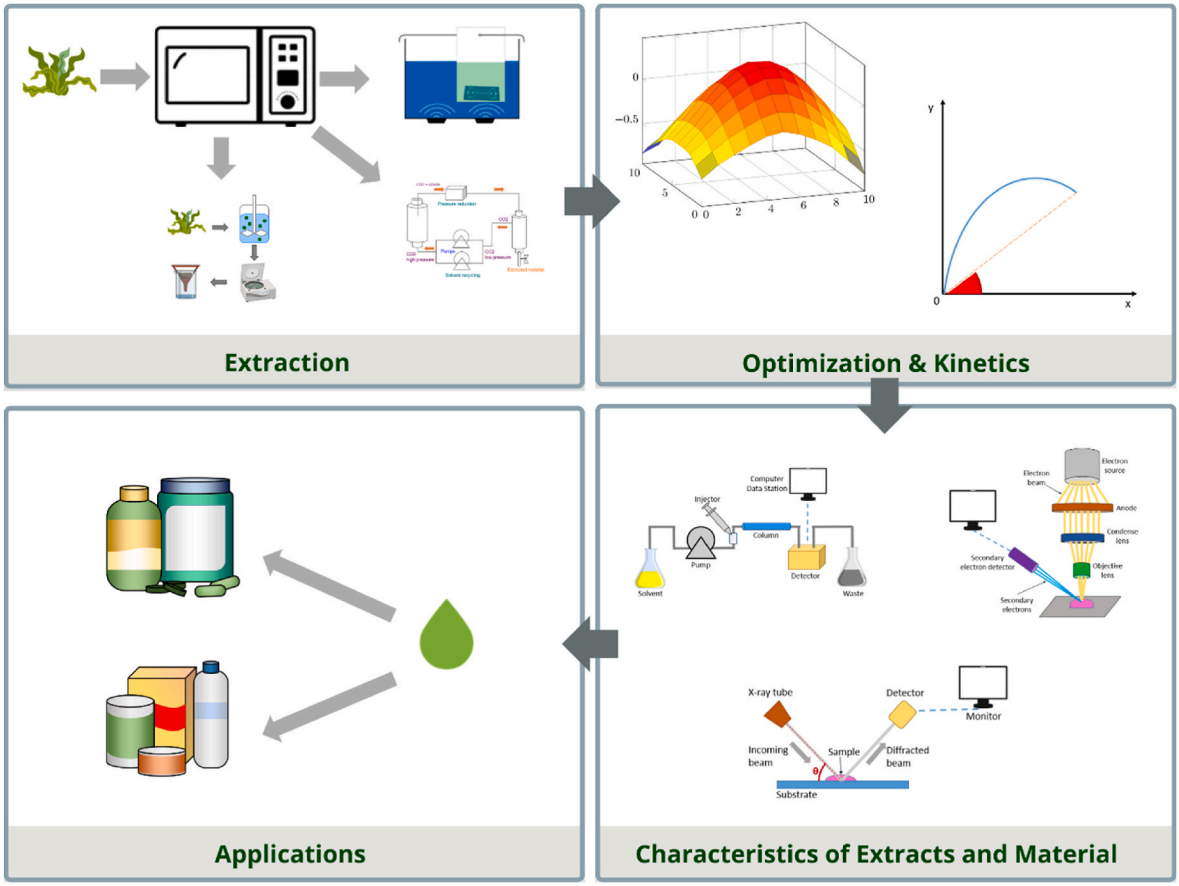

Fig. 6. The proposal for the double-stage extraction using MAE as a pretreatment method and the application of extracts in food products.

the dielectric constant of NADES in a multi-stage extraction method using MAE as the pretreatment process in future research.

- Then, the dynamic simulation and modeling should be quantified to detect the mechanism of multi-stage extraction. The effect of conditions in multi-stage extraction techniques on the recovery yield of BCs should be investigated and evaluated. Tan Phat Vo et al., 2024 investigated the effects of NADES-based ultrasonic-microwave-assisted extraction (UMAE) conditions on the recovery yield of BCs from *Codonopsis pilosula* and its mechanisms using the second-order extraction kinetic model. The author reported that the initial UMAE rate of terpenoids was 119 mg/g.min, which was higher than UME and MAE at 70 and 104 mg/g min, respectively. The researcher also investigated the effect of time and LSR on the recovery yield [114]. It can be concluded that the multi-stage extraction method has a higher extraction yield than single techniques. However, the effect of other conditions, such as water content, was not investigated. Therefore, this model can be applied in extracting algal compounds using multi-stage extraction techniques, and the effect of various conditions should be investigated in future research.
- Additionally, the detailed profiles of bioactive components should be determined using high-performance liquid chromatography/mass spectrometry (HPLC-MS) and gas chromatography/mass spectrometry. Gulden Goksen 2023 used HPLC-MS to clarify the phenolic profile of *Laurencia papillosa* using HPLC/MS and comparing the phenolic profile and content acquired from UAE and conventional extraction. There was no difference in the phenolic profile acquired from the two techniques, in which the feature phenolic substances were p-hydroxybenzoic acid, p-hydroxybenzaldehyde, quercetin caffeoyl-glucoside, and p-coumaric acid methyl ester [115]. Therefore, investigating the phenolic profile is necessary for investigating the profile of bioactive substances in multi-stage extraction processes. The difference in phenolic profile in multi-stage and single-stage techniques should be conducted in future research.
- The variation of surface morphology and cellulose crystallinity index before and after multi-stage treatment should be examined using scanning electron microscopy (SEM) and X-ray diffraction. Zebin Guo et al., 2019 investigated the surface morphology of sweet potatoes using SEM when they were treated with hot water extraction, MAE, UAE, and UMAE. The author reported that UMAE caused the largest deterioration on the cell wall surfaces of materials due to the synergy of ultrasound and microwave [116]. However, SEM and X-ray diffraction have not been used to investigate the surface morphology and crystallinity of algae after treatment with multi-stage techniques. Therefore, the research approach should be conducted in future research related to the extraction of BCs from algae using a multi-stage method.
- The usage of BCs from algae for developing food products is also a promising research interest, paving the way for using algal extracts on the industrial scale. The environmental influence and economic possibilities should be considered. Abirami Ramu Ganesan and Munisamy Shanmugam 2020 applied extracts with rich phycoerythrin to ice cream. The author reported that the total solid content of ice cream rose by 15.29 % compared to ice cream without added phycoerythrin extracts [117]. In addition to extracts, the algae biomass is directly added to yogurt, spreadable processed cheese, and colored yogurt [118–121]. This research demonstrated the potential for the application of algae extracts and biomass in food products at the laboratory scale, which makes way for applying them at the industrial scale.
- Additionally, the combination of advanced process monitoring and control techniques can track and streamline extraction processes. The collection and analysis of real-time information can give insights into the solubility of bioactive compounds and extraction kinetics. Such actions can enable dynamic adjustments to extraction conditions and ensure product quality on a large scale. Moreover, green extraction methods are suitable for circular economy principles, investigating tactics for waste valorization. The waste after extraction can used as biofertilizers, addictives, and energy sources, which enhances the sustainability and resource efficiency of the extraction process.

It is necessary to establish regulations to ensure algal extracts' safety when they are converted into food-grade ingredients. However, ensuring this transformation and following food safety requirements are problematic issues. In addition, studies concentrating on algae extracts' microbiological and toxic issues are lacking. For the industrial-scale production of algal extracts, their safety should be first evaluated, and the standards from food regulatory authorities in each nation should be established to ensure the quality of the usage of algal extracts such as food [122]. It is critical to consider the large-scale production feasibility of algal extracts in various aspects, including economy and technology before they are manufactured. For instance, the manufacturer should estimate the cost of raw materials, energy, and equipment, especially the MAE-SFE process, before extracting the BCs from algae. The extraction efficiency and toxicity for each type of material should be investigated. Additionally, the risks related to the operation, such as high pressure and temperature, should be considered and controlled by strict procedures and high technology, such as artificial intelligence.

The applications for the bioactive compounds extracted using green solvents are various. In our view, applying the bioactive compounds extracted using green solvents in the food sector is the most promising. Bioactive compounds extracted by NADES have high stability and potential as natural replacers for synthetic food preservatives. They act as scavengers, reacting with free radicals. These radicals are the main contributors to fat oxidation and protein degradation. Moreover, bioactive compounds extracted by NADES have antibacterial activity, inhibiting the proliferation of bacteria. These compounds open bacterial cell membranes and interfere with their metabolism, precluding food-borne illness and ensuring food safety for human consumption [123]. For example, 23.22 % tea saponins were obtained from *Camellia oleifera* with ternary NADES, which consisted of L-proline, glycerol, and sucrose at a 4:10:1 M ratio. The extraction process is supported by ultrasound at 100 W and 60 °C for 30 min. The antioxidant capacity of NADES-based tea extracts was 30.24 %; therefore showing its potential candidate as a natural food additive [124]. The other industries that benefit from these advances are the cosmetics and pharmaceuticals industries. In the cosmetics industry, active personal care components should obey restrictive regulations and meet different growing requirements related to naturalness, environment, and biodiversity preservation [125]. The restriction of creativity for years in the cosmetics industry is the safe orientation of benefit/risk balance, which is the main source of technological innovation. The cosmetics industry finds to enhance the sensible use of renewable materials via an effective sourcing stratergy. The quantity of extraction solvents to obtain algae extracts in the cosmetic field has decreased with rising sustainable requirements. Therefore, NADES rapidly show a potential to bring novelty. NADES-based extracts have a great compatibility with skin cells and bio-effectiveness which have in several categorial cosmetic claims (anti-aging, moisturizing, and anti-blue light). Additionally, the extraction process of NADES is driven by their hydrogen bond structure. Cosmetic formulations have a large figure for water. When NADES-based extracts are added in water-based formulations, their hydrogen bond structure is destroyed, resulting in the widespread distribution of bioactive compounds [126].

7. Conclusion

The study compiles the systematical knowledge related to the green solvent-based novel extraction techniques to recover BCs from algae. The UAE technique is based on the cavitation effect to facilitate the recovery of bioactive components. The microwave generates the heating effect via the oscillation and collision of polar molecules when these molecules absorb electromagnetic waves. The high temperature

evaporates water molecules in the algal matrix, which increases local pressure. The high pressure disrupts the algal cell wall, increasing the extraction yield. The EAE employed carbohydrase and protease to degrade the algal cell wall component, facilitating BCs' recovery yield. SFE employs the supercritical and subcritical states of substances, which possess the high diffusivity of gas and solubility of liquid. These properties can facilitate the acquisition of BCs from algae. The multi-stage extraction method should be developed to improve the extraction efficiency of bioactive components. The optimization of parameters in multi-stage extraction techniques should be investigated before conducting these techniques at large scales. These techniques, combined with green solvents, promise to improve sustainability, greenness, and safety when applied to recover bioactive components from algae in the food industry.

CRediT authorship contribution statement

Tan Phat Vo: Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Dinh Quan Nguyen:** Writing – review & editing, Supervision. **Thai Anh Thi Ho:** Visualization. **Thuan Minh Nguyen:** Visualization. **Nguyen Minh Huy Ha:** Visualization. **Phong H.N. Vo:** Writing – review & editing, Supervision.

Ethical guidelines

Ethics approval was not required for this research.

Data availability statement

All data generated or analyzed during this study are included in this published article.

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There are no funding sources for the manuscript.

Declaration of competing interest

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.

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Data availability

Data will be made available on request.

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