

Chapter 20

Efficient Production of Functional and Bioactive Compounds and Foods for Use in Food, Pharma, Cosmetic and Other Industries



Avi Shpigelman and Zoya Okun

1 Introduction

1.1 *Natural Bioactive Compounds and Their Sources*

Bioactive compounds are described as essential and nonessential compounds (e.g., vitamins or polyphenols) that occur in nature, usually are part of the food chain, and can be shown to promote human health. They are referred to as nutraceuticals that are present as natural constituents in food and provide health benefits beyond the basic nutritional value of the product (Biesalski et al. 2009). Natural bioactive compounds are characterized by a broad diversity of molecular structures and functionalities that provide an arsenal of components that can be utilized for the production of food additives, nutraceuticals, key components in pharma and cosmetic industries, and more. Some of the bioactive compounds can be found in nature at relatively high concentrations, but others can only be found in very limited quantities. Due to the complicated, time demanding, and often unprofitable organic synthesis, as well as the consumers' growing demand for the utilization of natural products having a clean label, massive plant harvesting is needed for obtaining sufficient amounts of the desired bioactive compounds. The challenges in the isolation and purification of these compounds contributed to the development of advanced processing methods and novel technologies based on pressure, mechanical, electrical, and thermal effects, as will be presented and discussed. The final yields of bioactive compounds extracted by various methods and technologies can be controlled and improved by the solvents variability, incubation times, and temperature steps, as well as by combination with enzymatic treatments, novel and green extraction procedures capable of improving the mass transfer of the bio-actives from the matrix,

A. Shpigelman · Z. Okun (✉)

Faculty of Biotechnology and Food Engineering, Technion, Haifa, Israel

e-mail: gzoya@bfe.technion.ac.il

the combination of several extraction technologies for a more efficient and satisfactory result is also widely examined. A great variety of bioactive compounds are extracted from agricultural produce, food wastes, and industrial by-products are widely explored. Among them are vitamins, pigments, lignans, polyphenolic compounds, carotenoids, bioactive oligosaccharides, and more. Few recently published examples of studies focusing on extraction of bioactive compounds, their sources, and suggested utilization are presented in Table 20.1.

This chapter will focus on various extraction techniques of bioactive compounds from two diverse families as model components based on aqueous solubility: (1) extraction of polyphenols from grape seeds and skins as a source of hydrophilic bioactive compounds and (2) Astaxanthin, a member of the carotenoid family, as a representative of the lipophilic bioactive compounds.

Global grape production reached 77.8 million tons in 2018, with China, Italy, Spain, and France being the major producers, and more than 70% of the grapes utilized for wine, must, and juice production (International Organisation of Vine and Wine 2019). One of the major by-products in the wine and juice industry are grape seeds, which can provide a rich source for lipids, proteins, carbohydrates, and flavonoids that are well-known polyphenolic antioxidants. Oil, extract and flour are the three products derived from grape seeds and further utilized by various industries. The extract consists of antioxidant compounds, possessing a vast assortment of health-promoting capabilities such as anti-inflammatory, anti-bacterial, and antiviral effects mostly attributed to the high polyphenolic content of the extract. During the years, more than 8000 polyphenolic compounds have been identified, and a broad range of beneficial activities was reported, highlighting the promising role of these compounds in the prevention of chronic, neurodegenerative, and cardiovascular diseases and for their antioxidant and anti-inflammatory activities (Denaro et al. 2020).

Table 20.1 Types of bioactive compounds from natural sources and their utilization

Source	Bioactive compound	Utilization	Reference
Red wine pomace	Polyphenols	Antioxidants	Croxatto Vega et al. (2021)
Cluster mallow	Natural pigment	Pigment for dye-sensitized solar cells	Golshan et al. (2020)
Mushroom waste	Vitamin D ₂ , ergosterol	Dietary supplement	Papoutsis et al. (2020)
Aloe	Polysaccharides	Prebiotic	Liu et al. (2021)
Sesame seed	Lignan	Antioxidant	Eom et al. (2021)
Guava's pulp and waste powders	Carotenoids	Lipophilic antioxidants	Da Silva Lima et al. (2020)
Stevia rebaudiana Bertoni	Steviol glycosides	Sweetener	Ahmad et al. (2020)
Crustacean by-products	Astaxanthin, lipids	Antioxidant, pigment	Ahmadkelayeh and Hawboldt (2020)

Astaxanthin is a carotenoid bioactive, part of a large group of lipophilic health-promoting components. This orange-reddish pigment is biosynthesized in various microorganisms. It has a high antioxidant capacity and was reported as an immune response enhancer, contributed to an improvement of skin health and tissue damage, reported to play a role in the treatment of diabetes and cardiovascular diseases, presented anticarcinogenic properties, and much more. The beneficial and promising results were also presented in human clinical trials (Donoso et al. 2021). In nature, astaxanthin is synthesized by microorganisms, both aquatic and non-aquatic, such as bacteria, fungi, yeasts, and microalgae. Its production and extraction from natural sources is being explored due to the consumers' concern regarding synthetic food additives and the demand for clean label and healthier food. The main source of astaxanthin for extraction is the freshwater green microalgae *Haematococcus pluvialis* which is recognized by FDA as a safe astaxanthin source for human consumption.

Astaxanthin contains 40 carbon atoms with two terminal ring systems joined by a chain of conjugated double bonds, responsible for light absorbance in the visible region (~500 nm) and results in characteristic red color (Higuera-Ciagara et al. 2006). Astaxanthin has two chiral centers at positions C-3 and C-3' (marked red in Fig. 20.1), resulting in a mixture of two enantiomers (3S,3'S & 3R,3'R) and the *meso* form (3R,3'S) as presented in Fig. 20.1. It can be produced naturally by extraction from microorganisms or chemically synthesized. In recent years, the market for natural astaxanthin has been growing substantially, with a purity dependant value varying from 2500 to 7000 USD/kg to about 15,000 USD/kg for human

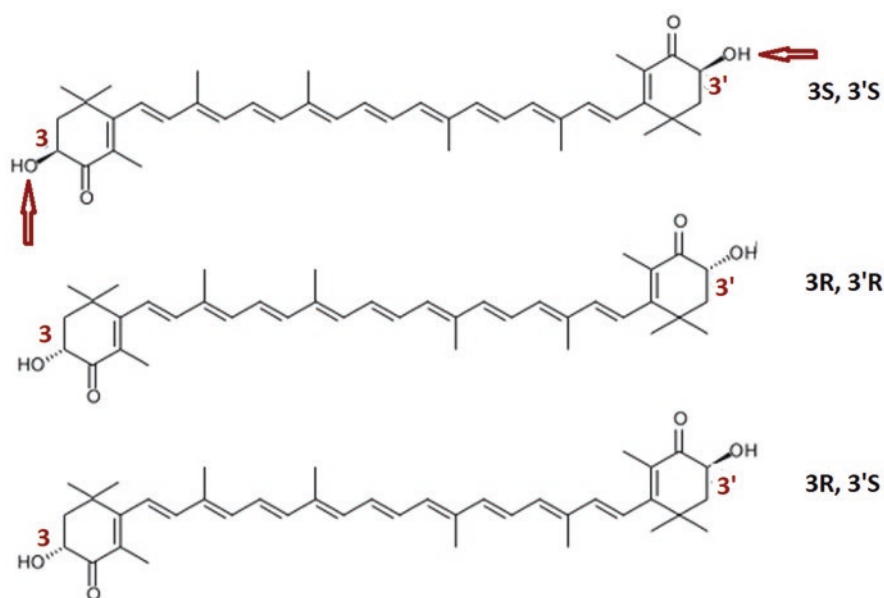


Fig. 20.1 Astaxanthin stereoisomers, esterification sites marked by arrows

applications such as cosmetics, food, and dietary supplements. The synthetic compound is less expensive ~1000\$/kg, but is not approved for human consumption and is usually utilized in animal feed (Rodríguez-Sifuentes et al. 2021). The main differences between natural and synthetic astaxanthin are (1) Esterification degree, the natural extract will usually be found in mono or di-ester form, while the synthetic compound will be in its free unesterified form (esterification sites marked by red arrows in Fig. 20.1) and (2) Stereochemical composition, the synthetic form consists of a mixture of isomers in ratio 1:2:1 (3S,3S), (3R,3S), and (3R,3R) respectively, while the composition of natural extract depends on its source. These differences are suggested to affect the health-promoting performance of the synthetic compound.

The goal to extract astaxanthin from natural sources more competitively when compared with the synthetic route is challenging due to the need to overcome the critical points related to biomass concentration, the environmental impact, and product stability, compromising yield and quality of the extracted material.

The reviewed in this chapter technologies may provide an innovative and economical approach for the enhanced production of bioactive compounds for use in food, pharma, cosmetics, and other industries.

2 Industrial Utilization of Bioactive Compounds (Example of Grape Seed Polyphenols and Astaxanthin)

The global market for Carotenoids reached \$1.5 billion in 2017 and expected to reach \$2.0 billion by 2022, at a compound annual growth rate (CAGR) of 5.7% for the period of 2017–2022, while the astaxanthin market only was valued at 512.8 Million USD in 2016 and projected to grow at a CAGR of 6.73% from 2017, to reach a projected value of 814.1 million USD by 2022 (McWilliams 2018). The driving factors in the astaxanthin market are a high demand due to its antioxidant properties and increasing applications in the aquaculture industry, growing demand for natural food coloring agents with lesser adverse effects as compared to other chemical products, are the key factors estimated to boost the continues market growth. Some of the players in the astaxanthin market are Alga Technologies; Cyanotech Corporation; Fuji Chemicals Industries Co., Ltd; Fenchem; Beijing Gingko Group (BGG) (Astaxanthin Market Size 2020–2027). Astaxanthin derived commercially available products can be found in the form of capsules, powders, soft gels, oil extracts, and creams, few examples of such products are presented in Table 20.2.

As mentioned before, grape seed extract is an industrial derivative of grape seeds. It is rich in antioxidants and oligomeric proanthocyanidin complexes and has been linked to a wide range of potential health benefits. The grape seed extract is available as a dietary supplement in a liquid form, tablets, or capsules. Supplements commonly contain 50–100 mg of the extract. Few studies also suggested the

Table 20.2 Variety of astaxanthin derived products

Manufacturer	Brand name	Form	Astaxanthin content	Application
Algatech	Astapure®	Oleoresin	5%, 10%, 20%	Topical cream, emulsions
Solgar	Natural astaxanthin	Soft gel	5 mg	Antioxidant support, Skin health
Cyanotech	BioAstin®	Capsule	4 mg	Food supplement
BGG	AstaZine®	Powder	2%	Antioxidant
True Botanica	Face Cream – with Astaxanthin	Cream	n.a.	Face moisturizing cream
Astalif	Astaxanthin	Soft gel	12 mg	Antioxidant, food supplement
Sinacon	Red plus+	Powder	n.a.	Color enhancer, fish food additive

utilization of grape seed extracts not only as a food additive with health-promoting capabilities, but also as potent dyes and flame retardants in the fabric industry (Guo et al. 2020), and as functional ingredients in meat and fish products (Mainente et al. 2019).

3 Technological Methods for the Production of Bioactive Compounds

Among the common methods used for the extraction are the conventional liquid-liquid or solid-liquid extraction utilizing a broad range of organic solvents by the principle of Soxhlet extraction (Fig. 20.2). Soxhlet is an apparatus utilized for one of the most conventional extraction methods in the case of solid-liquid extractions (also named leaching especially in industrial applications) and usually serves as an accepted standard for comparison with other extraction approaches. In this technique, the plant matrix containing the bioactive compounds is placed into a disposable thimble, positioned in the soxhlet apparatus as presented in Fig. 20.2. The extraction solvent is added to the flask and being refluxed, the vaporized solvent rises in the vapor tube, and cooled by the condenser circulated with cooling water. The condensed solvent flows back into the thimble containing the sample and dissolves the bioactive compounds. Once the siphon is filled, the solvent with the extract is transferred back to the flask. The extraction solvent is continuously cycled through the plant matrix, by boiling and condensation, with the bioactive compounds being extracted and collected in the flask.

Soxhlet method used as a batch process on small scales, and converted into a continuous extraction procedure on medium or large scales. Among the samples for industrial leaching equipment are Bollman, Rotocel and Kennedy extractors (Smith 2011).

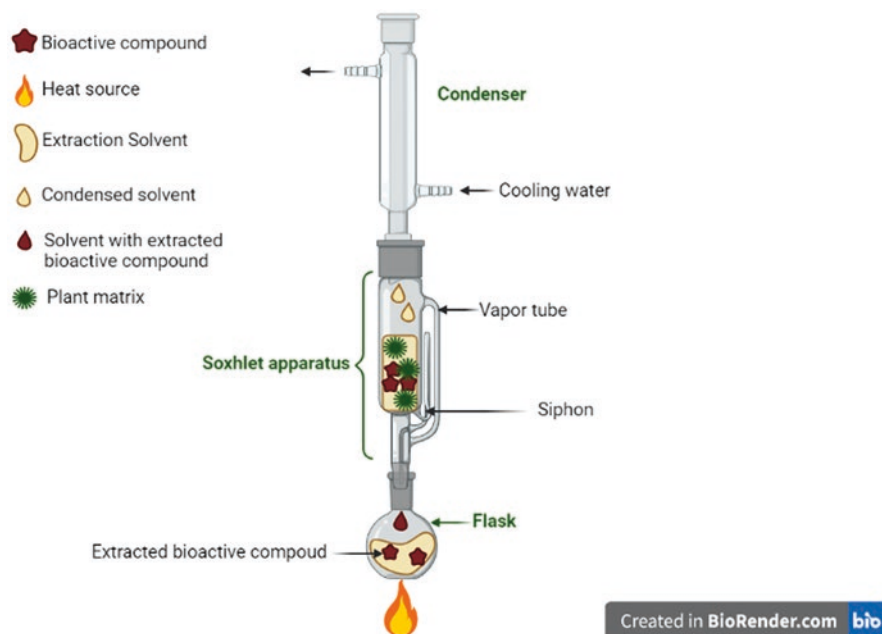


Fig. 20.2 Operation principle of the Soxhlet apparatus

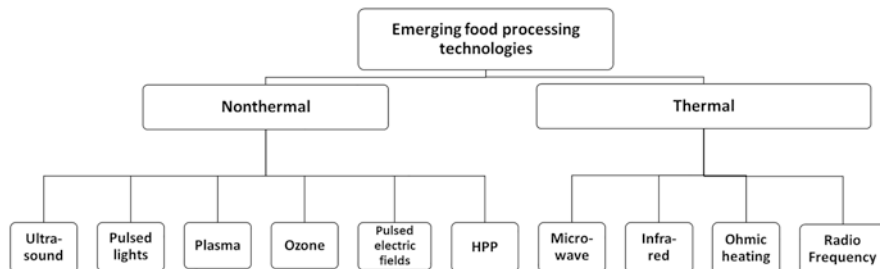


Fig. 20.3 Emerging processing technologies studied for potential to support extraction

Among the drawbacks of Soxhlet is the elevated solvent temperatures used for efficient extraction which makes this method incompatible with thermally sensitive bioactive compounds, long extraction times, utilization of organic solvents accompanied with the need for complete further removal due to their toxicity and their negative environmental impact, as well as high cost of the solvents and their time demanding evaporation.

The emerging processing technologies developed and optimized during the years are classified as thermal and nonthermal methods (presented in Fig. 20.3), in the field of extraction the leading representatives are high pressure, microwave and ultrasound-assisted extractions, pulsed electric field assisted extraction and more.

While the nonthermal technologies often include a partial thermal aspect, this aspect is not suggested to be the main one responsible for the beneficial effect.

3.1 Non-thermal Technologies

Due to the increased consumer demand for high-quality foods, new technologies were developed and introduced to the food industry, in many cases for microbial inactivation and shelf life enhancement, and some of these technologies were explored and found useful for improved extraction of bioactive compounds. The advantages of such technologies are often the improvement of matrix disruption, lower processing temperatures, and/or shorter treatment times, which is highly favored for thermolabile compounds. In addition, they can in some cases replace the need for organic solvents. The leading representatives among the nonthermal (or partially thermal) technologies are Pulsed Electric Fields (PEF), Ultrasound (US), and High Hydrostatic Pressure (HHP). In the following section, we will review some of the nonthermal technologies and their most recent utilization for the extraction of astaxanthin and polyphenols.

3.1.1 Pulsed Electric Fields (PEF)

The operation principle of PEF is the application of high voltage pulses to permeate cell membranes or to increase membrane porosity (electroporation). Electroporation is defined as the process of pore formation in cellular membranes due to the utilization of an electric field. This technology involves the operation of high voltage electrical pulses, typically with a field strength from 0.5 to 20 kV/cm to samples/products placed in PEF chamber between two electrodes for a short time (10^{-5} – 10^{-2} seconds) to avoid a significant heating effect. Exposure to an external electric field induces the increase of transmembrane potential due to the charges of opposite polarities from both sides of the cell membrane, the electrostatic attraction between the opposite charges results in the formation of pores in the membrane favoring the release of intracellular valuable contents (Fig. 20.4a). Among the parameters affecting the extraction efficacy are electric field intensity, reaction time, number of pulses, pH, and ionic strength of the solvent.

PEF was recently utilized for the extraction of astaxanthin from *H. pluvialis*. Various PEF treatment times, number of pulses, and field strengths were examined to identify optimal conditions. The treatment of 10 pulses 1 kV/cm for 5 ms each at 20 °C resulted in 1.2-fold more efficient extraction compared to classical disruption methods like bead-beating, freezing-thawing, thermal treatment. In this research cells treated by PEF were incubated for 6 hours in a growth medium at room temperature in the absence of light, after the incubation the suspension was centrifuged, and the biomass was resuspended in ethanol that was identified as the optimal

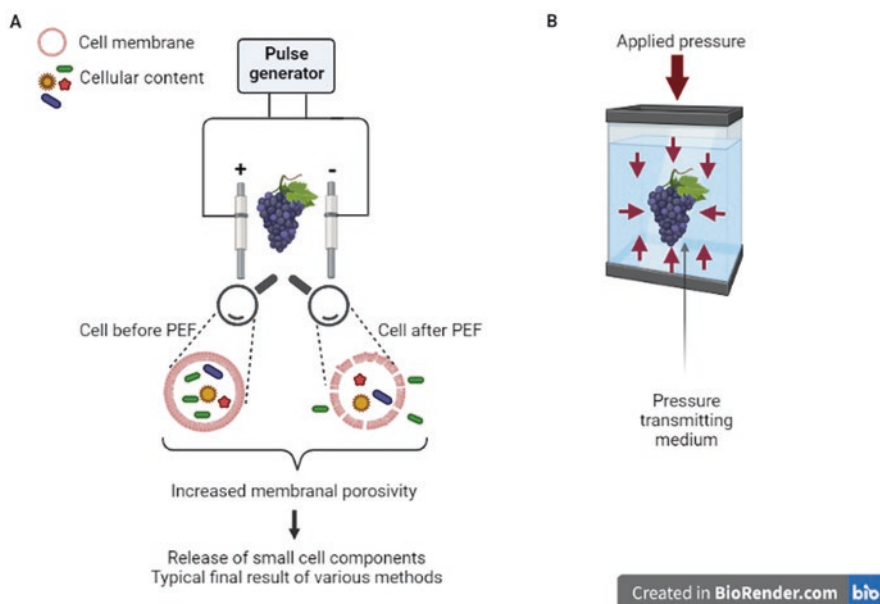


Fig. 20.4 Schematic operation principle of PEF (a) and HHP (b) assisted extraction

extraction solvent, this resulted in remarkable extraction of 96% carotenoid content compared to 80% using other physical methods (Martínez et al. 2019).

3.1.2 Ultrasound (US)

The operation principle of US is based on the acoustic cavitation phenomenon generated by the sound waves in the range of 200–100 MHz. Ultrasonic cavitation leads to extreme temperatures, yet only locally, pressure differentials, and high shear forces. When cavitation bubbles implode on the surface of plant cells, the perforation of cell walls and cell membranes takes place and cell disruption occurs. The mechanical effects of ultrasound-induced cavitation, intensify the penetration of the solvent into the cell interior and improves the mass transfer between cell and solvent so that the intercellular materials are transferred into the solvent affecting the extraction efficiency. Among the main parameters affecting the extraction efficacy, are matrix factors like particle size and moisture content, process factors like power and reaction time, and solvent factors like polarity and viscosity. The two most popular and researched goals for extraction modes for ultrasound-based instruments are an ultrasonic probe system, where the probe is inserted directly into the sample and an ultrasonic water bath where no direct contact between the sample and the probe occurs.

Ultrasound was recently utilized for the extraction of polyphenols from grape seeds. Kinetic studies aiming for an optimized industrial implementation suggested

that the optimal model includes parameters such as hydrodynamics, mixing, and mass transfer which control the effectiveness in the physical/chemical processing applications. Such a methodology can promote optimal economic scale-up strategies required for the industrial application of ultrasound assisted extraction.

In extraction trials, aliquots of grape seeds were mixed with several solvents at different extraction conditions. The ultrasonic probe was placed at the center of the extraction vessel and submerged about 5 cm under the mixture surface. The best extraction yield of TPC for all the samples was obtained using UAE with an ethanol-water mixture (57:43 v/v) as the solvent, at 50 °C, 200 W and 26 kHz after 30 min (Natolino and Da Porto 2020).

3.1.3 High Hydrostatic Pressure (HHP) and High Pressure Homogenization (HPH)/(UltraHPH)

HHP is a non-thermal technology increasingly used in the food industry as a cold pasteurization method. Its operation is based on Pascal's principle where an applied change in pressure is transmitted uniformly and immediately in the high-pressure vessel containing the product in a vessel filled with pressure-transmitting medium (Fig. 20.4b). By subjecting the product, usually in the final package, to elevated pressures up to 1000 MPa (industrially up to 600 MPa) for a short holding time (mostly 3–5 min) pathogens and spoilage bacteria can be inactivated, while effects on low-molecular-weight molecules (e.g. sugar, vitamins, pigments, flavor compounds) are minimal. High hydrostatic pressure can damage cellular membranes, disrupting tissues and organelles, thereby favoring the release of bioactive compounds.

Homogenization is a physical process in which a dispersed system, suspension or emulsion, is forced to flow at a high velocity through a narrow passage, a disruption valve, producing a smaller and narrow particle size distribution. High-pressure homogenization (HPH) is one of the emerging technologies being studied and developed for various applications in the food industry. It was suggested as an effective tool for achieving microbial safety and extending the product shelf life of liquid foods in a continuous process while minimizing some negative attributes of thermal processing. The valve geometry, pressure level, inlet temperature, and the number of homogenization cycles are all factors affecting the level of microbial inactivation and the extent of the impact on techno-functionalities of food biopolymers and matrices. Turbulence, high shear, cavitation, and temperature increase induced by HPH treatments enhance emulsion stability, stabilize proteins in solutions, reduce particle size distributions, and increase the accessibility of health-promoting compounds. A major difference between HPH and conventional homogenization is the maximum pressure level reached, and it is dependent on the homogenizer design and characteristics such as gap size, seals, and valve geometry. Ultra HPH reaches pressure levels up to 400 MPa, while HPH is usually defined to reach pressure levels between 50 and 200 MPa.

Recently HPH was utilized for exploring morphological changes and cell disruption of *H. pluvialis* cells for astaxanthin extraction. When pressures of 10,000–30,000 psi (~70–200 MPa) were applied the intact cyst cells were significantly disrupted or fully ruptured, releasing the cytoplasmic components, thereby facilitating the extraction and successful separation of astaxanthin. Number of passages (cycles) of HPH (1–3 times) could significantly improve the cell disruption efficiency. The maximum astaxanthin recovery was estimated to be 1.1% (weight of dry cells) (Praveenkumar et al. 2020).

3.2 Thermal Technologies

3.2.1 Microwave (MW)

Microwaves are part of the electromagnetic spectrum in the frequency range 300 MHz–300 GHz (Fig. 20.5c). The operation principle is based on magnetic and electric fields acting on components with the ability to convert the absorbed energy to heat. The induced energy is further transferred via dipole rotation and ionic conduction. In the plant matrix, the moisture evaporates due to the adsorption of electromagnetic energy. Evaporation leads to pressure generation inside the cell resulting in swelling and structural changes improving the porosity of the matrix which favors

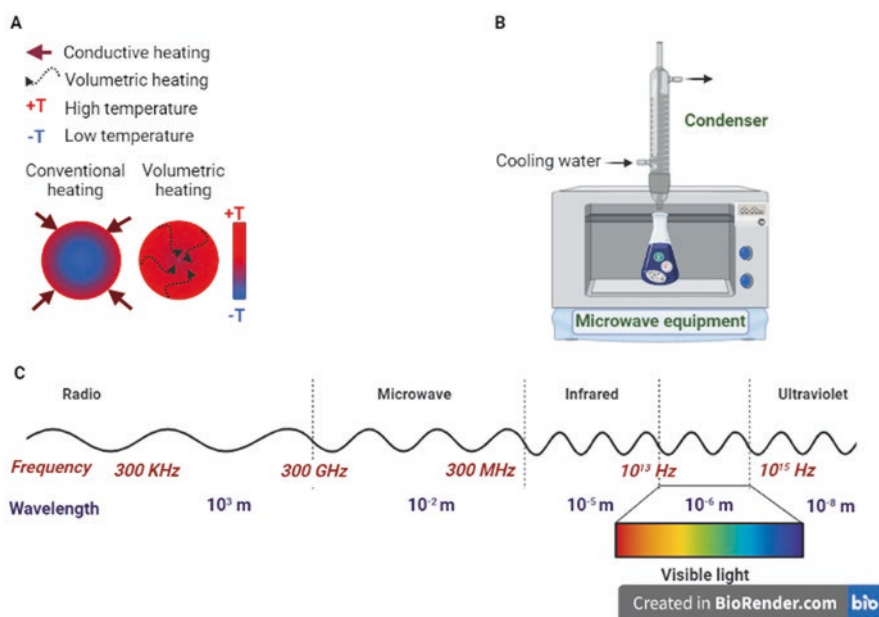


Fig. 20.5 Schematic representation of conventional and volumetric heating principle (a), microwave equipment for assisted extraction (lab scale) (b), part of the electromagnetic spectrum (c)

mass transfer and better extraction of the bioactive compounds. Schematic representation of microwave-assisted extraction procedure is presented in Fig. 20.5b.

Recently a study involving microwave-assisted extraction was published dealing with the combined effects of various techniques and compares it to traditional Soxhlet extraction. The combined enzymatic, microwave and salting-out extraction method has been developed and evaluated as an effective method to extract polyphenols from grape seeds. The results showed that different extraction methods not only affect the extraction yield of polyphenols but also have significant effects on the composition of monophenols. Ten kinds of monomer phenolic compounds were analyzed by HPLC, only four were identified by Soxhlet extraction vs eight different monomeric phenolic compounds with antioxidant activity that were extracted by combined techniques (Jia et al. 2021).

3.2.2 Ohmic Heating (OH)

OH (also termed Joule heating) is based on the application of an alternating electric current for rapid and evenly distributed heat generation. In accordance with Ohm's law, the amount of energy (dissipated heat) is related to both applied voltage and electrical conductivity of the treated matrix. Due to the thermal destruction, the permeability of the cell membrane increases leading to the promotion of the extraction of bioactive materials from the plant matrix.

Ohmic Heating was utilized for the extraction of anthocyanins, from winemaking residues by using the grape skins as natural electrical conductors allowing the internal heat dissipation through OH. Recently, several processing parameters were evaluated: (1) mild temperatures at 40 °C during 20 min; (2) flash heating from 40 to 100 °C in less than 20 s. These treatments were followed by aqueous extraction in water at room temperature. Independently of the temperature applied, OH allowed boosting extraction levels, increasing concentration of total phenolic compounds, soluble solids, and red color intensity of the obtained extracts. OH treatments at high-temperature short-time (HTST), due to the fast internal heating of grape skin structure, resulted in an increase of total concentration of anthocyanins from 756 to 1349 µg/g, with malvidin-3-O-glucoside being the main compound identified and quantified in the aqueous extracts (corresponding to about 60% of the total). These results reveal that OH might be considered an efficient and environmentally friendly technology to improve the extraction of polyphenolic compounds. Due to the volumetric heating effect, the OH technique reduces treatment times and the use of water and lowers energy consumption when compared with conventional thermal processes, furthermore, it can assist in avoiding the use of organic solvents. The authors suggested that the flash-heating extraction process allows permeabilization of tissues without promoting thermal degradation of the bioactive compounds (Pereira et al. 2020).

3.2.3 Infra-red (IR)

The infrared electromagnetic spectrum ranges from 0.75 to 1000 μm . Infrared-assisted extraction, utilizes the IR wavelengths to achieve a required heating effect. During infrared-assisted extraction, the heating leads to cell bursting. Internal heat is generated as a result of molecular collisions that absorb and dissipate energy from the electromagnetic field. The high efficiency of this technology is attributed to the high capacity of IR penetration. Infrared radiation can achieve high efficiency by matching the wavelength to the material absorption characteristics. Infrared has been widely explored for the extraction of bioactive compounds from medicinal herbs with the advantages of shorter time, high efficiency, simple operation, and environmental safety.

IR assisted extraction was utilized for the extraction of catechin, epicatechin, and procyanidin B2 from grape seeds. Three factors were examined for process optimization, (1) solvent, (2) solid/liquid ratio, and (3) illumination time. The chosen infrared-assisted extraction conditions were: 50% methanol solution as extraction solvent, solid/liquid ratio of 1:150 g/mL, and illumination time of 30 min. The extraction efficiency of IR was compared with microwave-assisted extraction (MW), ultrasonic extraction (US), and classical electrical heating (CH) methods, the results are summarized in Table 20.3. The IR method was found as the most effective. This might be explained by the infrared wave possessing a unique heating mechanism resulting in cell bursting which was created during the infrared heating. Cell bursting favors the entry of extracting solvent leading to solubilization of the target molecules. The solution of 50% methanol is a polar extraction solvent that can efficiently absorb infrared wave energy and leads to efficient heating, which eventually results in cell walls rupture. The IR extraction yield of epicatechin was found to be higher than for US (ultrasound), but lower than for MW (microwave). The reason for this phenomenon (the modification of not only total yield but also the ratio between components) may be related to the molecular structure of the extracted

Table 20.3 Comparison of various extraction methods re. polyphenols extraction from grape seeds

Extraction method	Catechin(mg/g)	Epicatechin (mg/g)	Pro. B3 (mg/g)	Examined parameters	Optimal conditions
MW	37	33	10	Solid/liquid ratio, power, working time	1:50, 600 W, 11 min
IR	47.9	30	12.1	Solvent, solid/liquid ratio, illumination time	50% MeOH, 1:150, 30 min
US	36	27	12	Solid/liquid ratio, power, working time	1:50, 90 min, 90 W
CH	30.7	26	7.2		n.a.

Data from Cai et al. (2011)

MW microwave, IR infrared, US ultrasound, CH conventional heating

molecules. The results indicated that IR has a great potential for offering an alternative technique for extraction of bioactive compounds (Cai et al. 2011).

3.2.4 Radio Frequency Heating (RFH)

RFH like IR differs from conventional conduction or convection heating by heat generation within the sample (volumetric heating) (Fig. 20.5a). Radio frequency is the electromagnetic wavelength positioned in the range of 300 kHz to 300 MHz (Fig. 20.5c). Despite the broad frequency range, only three frequencies are legally allowed to be used in the US (13.56 MHz, 27.12 MHz, and 40.68 MHz) to avoid interference with telecommunications. Since the heat in this method is generated within the material, the time required to obtain the required heating is relatively shorter than the time needed by conventional heating methods. The internal heating assists in cellular deformation which allows the enhanced movement of compounds into the extraction solvent. RFH is known as more effective in the case of semi-solids than the conventional heating, because of a more homogeneous heat distribution inside the treated material. RFH efficiency depends on the electromagnetic properties and shape of the sample and electrodes specification.

4 Summary

Natural bioactive compounds are common in numerous plants, algae and microorganisms, but their amounts are usually limited. The utilization of waste and agro-industrial by-products as a rich source of natural bioactives is highly desirable, both in terms of economic and environmental impact and in terms of potential sources for recovery of desired compounds. A growing area of consumers' interest and expectation, when it comes to cleaner labels and natural food components, leads to the need to improve and enhance the extraction methods and technologies to become more environmentally friendly, faster and resulting in a more competitive process than the chemical synthesis. The traditional extraction techniques have gradually switched to novel extraction technologies developed for more efficient and facilitated extraction of bioactive compounds, based on thermal and non-thermal principles which are widely explored for recovery of various bioactive compounds from a vast majority of natural sources and waste streams. In this chapter, thermal and non-thermal technologies were introduced through the examples of polyphenol extraction from grape seeds-the waste of wine and grape juice industry, and astaxanthin extraction, both bioactive compounds known as potential antioxidants with various health-promoting activities and with different aqueous solubility. The innovative extraction technologies present advantages in terms of shorter reaction times, lower temperatures (of extreme importance in the case of thermolabile bioactive compounds), reduced volumes of environmentally non-friendly organic solvents, and higher yields and purity of the desired compound. Different extraction methods

not only affect the extraction yield but also have significant effects on the composition of the extract, possibly contributing to diversifying the bioactivity of the extract. Successful membrane permeability, improved diffusion, and enhanced mass transfer are among the main parameters involved in proper extraction. The novel technologies present a range of advantages in the field of bioactive compounds extraction, but significant knowledge gaps still exist, in particular, optimization of technological operation conditions relevant for industrial scales and levels.

References

- Ahmad J, Khan I, Blundell R, Azzopardi J, Mahomoodally MF (2020) Stevia rebaudiana Bertoni.: an updated review of its health benefits, industrial applications and safety. *Trends Food Sci Technol* 100:177–189
- Ahmadkelayeh S, Hawboldt K (2020) Extraction of lipids and astaxanthin from crustacean by-products: a review on supercritical CO₂ extraction. *Trends Food Sci Technol* 103:94–108
- Astaxanthin Market Size, Share | Industry Report, 2020–2027. <https://www.grandviewresearch.com/industry-analysis/global-astaxanthin-market>
- Biesalski HK et al (2009) Bioactive compounds: definition and assessment of activity. *Nutrition* 25:1202–1205
- Cai Y, Yu Y, Duan G, Li Y (2011) Study on infrared-assisted extraction coupled with high performance liquid chromatography (HPLC) for determination of catechin, epicatechin, and procyanidin B2 in grape seeds. *Food Chem* 4:1872–1877
- Croxatto Vega G et al (2021) Insights from combining techno-economic and life cycle assessment – a case study of polyphenol extraction from red wine pomace. *Resour Conserv Recycl* 167:105318
- da Silva Lima R, Nunes IL, Block JM (2020) Ultrasound-assisted extraction for the recovery of carotenoids from guava's pulp and waste powders. *Plant Foods Hum Nutr* 75:63–69
- Denaro M et al (2020) Antiviral activity of plants and their isolated bioactive compounds: an update. *Phytother Res* 34:742–768
- Donoso A, González-Durán J, Muñoz AA, González PA, Agurto-Muñoz C (2021) Therapeutic uses of natural astaxanthin: an evidence-based review focused on human clinical trials. *Pharmacol Res* 166:105479
- Eom SJ et al (2021) Development of an ultrasonic system for industrial extraction of unheated sesame oil cake. *Food Chem* 354:129582
- Golshan M, Osfour S, Azin R, Jalali T (2020) Fabrication of optimized eco-friendly dye-sensitized solar cells by extracting pigments from low-cost native wild plants. *J Photochem Photobiol A Chem* 388:112191
- Guo L, Yang ZY, Tang RC, Yuan HB (2020) Grape seed proanthocyanidins: novel coloring, flame-retardant, and antibacterial agents for silk. *ACS Sustain Chem Eng* 8(15):5966–5974. <https://doi.org/10.1021/acssuschemeng.0c00367>
- Higuera-Ciapara I, Félix-Valenzuela L, Goycoolea FM, Félix-Valenzuela L (2006) Astaxanthin: a review of its chemistry and applications. *Crit Rev Food Sci Nutr* 46:185–196
- International Organisation of Vine and Wine (2019) 2019 Statistical report on world vitiviniculture. 2019 Statistical report on world vitiviniculture. <http://www.oiv.int/public/medias/5029/world-vitiviniculture-situation-2016.pdf>
- Jia MZ, Fu XQ, Deng L, Li ZL, Dang YY (2021) Phenolic extraction from grape (*Vitis vinifera*) seed via enzyme and microwave co-assisted salting-out extraction. *Food Biosci* 40:100919
- Liu C et al (2021) Extraction, characterization of aloe polysaccharides and the in-depth analysis of its prebiotic effects on mice gut microbiota. *Carbohydr Polym* 261:117874

- Mainente F, Menin A, Alberton A, Zoccatelli G, Rizzi C (2019) Evaluation of the sensory and physical properties of meat and fish derivatives containing grape pomace powders. *Int J Food Sci Technol* 54:952–958
- Martínez JM et al (2019) Use of pulsed electric field permeabilization to extract astaxanthin from the Nordic microalga *Haematococcus pluvialis*. *Bioresour Technol* 289:121694
- McWilliams A (2018) Global carotenoids market research report to 2022. The global market for carotenoids. <https://www.bccresearch.com/market-research/food-and-beverage/the-global-market-for-carotenoids.html>
- Natolino A, Da Porto C (2020) Kinetic models for conventional and ultrasound assistant extraction of polyphenols from defatted fresh and distilled grape marc and its main components skins and seeds. *Chem Eng Res Des* 156:1–12
- Papoutsis K et al (2020) Recovery of ergosterol and vitamin D2 from mushroom waste – potential valorization by food and pharmaceutical industries. *Trends Food Sci Technol* 99:351–366
- Pereira RN et al (2020) Using Ohmic Heating effect on grape skins as a pretreatment for anthocyanins extraction. *Food Bioprod Process* 124:320–328
- Praveenkumar R et al (2020) Morphological change and cell disruption of *haematococcus pluvialis* cyst during high-pressure homogenization for astaxanthin recovery. *Appl Sci* 10:513
- Rodríguez-Sifuentes L, Marszalek JE, Hernández-Carbajal G, Chuck-Hernández C (2021) Importance of downstream processing of natural astaxanthin for pharmaceutical application. *Front Chem Eng* 2:29
- Smith PG (2011) Mass transfer operations. In: *Introduction to food process engineering*. Springer US, pp 437–465