

Editorial

Extraction and Isolation of Natural Products

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Bioactive compounds are substances that are generally found in small amounts in food and can have beneficial health effects [1]. Unlike essential macro- and micronutrients, such as proteins, carbohydrates, lipids, vitamins, and minerals, they are not indispensable for the survival of the organism. However, much of the literature data show the protective effects of these compounds on health but also countering cardiovascular diseases (CVD), cancer, and neurodegenerative diseases, although most of this knowledge derives from in vitro studies on human cell cultures and from animal studies [2–4]. In fact, the data deriving from the studies on the human organism are, to date, still limited, and this does not always allow definitive conclusions to be drawn. In addition, many of the studies that evaluate the effect of various bioactive compounds on health use foods that are particularly rich in them rather than isolated compounds. Therefore, it is difficult to establish whether the beneficial effects depend purely on a certain compound or on a synergistic action with the other compounds present in foods. Consequently, there are more and more lines of research directed towards the knowledge of bioactive compounds and their applications in various fields.

In many industrial processes, the initial phases for the realization of a product require the use of solid–liquid extraction techniques to obtain the bioactive compounds contained in the most varied matrices [5,6]. As is known, solid–liquid extraction is a separation technique used both in the laboratory and on an industrial scale to extract a compound or a class of compounds from a solid matrix using a solvent. To optimize the extraction process, some aspects need to be considered. It is important to know the physical and chemical properties of the matrix, such as melting temperature, mechanical properties, and solubility. The granulometry of the solid matrix must be checked and adapted to extraction. For example, a small particle size favors the dispersion of the solvent but could clog the extraction system, so it is necessary to find an adequate particle size for each process. Another important aspect is the choice of the solvent, based on the solute to be extracted (“like dissolves like”). The solvent must not react or dissolve the matrix, it must be selective towards the solute, and it must not be volatile. Therefore, choosing the suitable solvent that meets all the above requirements is a challenging task, as a compromise must be found between the process, the matrix, and the target molecules. The extraction techniques can be divided into conventional and innovative [7]. Conventional techniques generally do not require sophisticated equipment but have some disadvantages, such as the need for high amounts of solvent, low extraction selectivity, the need for long timing, and thermal decomposition for thermolabile compounds. Conventional extraction techniques are maceration, percolation, pressing, counter-current extraction, extraction through the Soxhlet, and distillation [8]. To date, conventional or solvent extraction protocols are still widely used in research and industry with satisfactory yields using relatively simple and cost-effective equipment. However, in recent times, new techniques have been developed to overcome the limitations of the aforementioned conventional methods. On the other hand, the innovative extraction techniques, introduced relatively recently in the industrial field, have numerous advantages, such as reduced energy consumption, the greater safety and control of the extraction technique, the reduction or elimination of the solvent, the satisfaction of the legal requirements regarding emissions, reduced costs, and



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the improvement of the quality and functionality of the entire process. Among other things, the extraction yields and recovery rates of bioactive compounds could be improved by suitably combining and integrating the extraction methods [9]. The innovative extraction techniques are: ultrasound-assisted extraction (UAE) which, through cavitation and the rupture of cell walls, reduces costs, time, and increases yield; extraction with supercritical fluids (SFE) which, thanks to the safety of the solvents used, has been recognized as a GRAS (generally recognized as safe) procedure by the FDA (Food and Drug Administration); microwave-assisted extraction (MAE), which guarantees maximum reproducibility and efficiency; accelerated solvent extraction (ASE) with reduced time and solvent consumption; solid phase extraction (SPE), the best known preparation technique used in clinical, environmental, and pharmaceutical chemical analyzes; solid-phase microextraction (SPME), a simple, sensitive technique that does not involve the use of solvents; rapid solid–liquid dynamic extraction (RSLDE) using Naviglio extractor, which allows extraction at room or sub-ambient temperature by exploiting an increase in pressure of the extracting liquid on the solid matrix to be extracted [10]. Therefore, to identify the most suitable extraction procedure, it is necessary to know the structure and composition of the active ingredients to be extracted, as well as the matrix that contains them. Furthermore, currently, to achieve a low environmental impact, in order for the extraction processes to be defined as sustainable, it is important to use technologies with high energy efficiency and which are based on low environmental impact solvents obtained preferably from renewable sources, according to a recent conception of chemistry, called green chemistry [11]. The latter aims to convert old technologies into new clean processes by preventing pollution, reducing or eliminating the use of hazardous substances, and developing products and processes that reduce the impact on the environment. Moreover, to date, under the environmentalist push, a new economic system based on the reuse of waste is spreading, according to the new concept of a circular economy. In this way, waste is reduced, and available natural resources are preserved [12,13]. Starting from these premises, many waste materials, in particular those coming from the agro-food sector, can represent a valuable source of bioactive compounds with different possible uses in the cosmetic, pharmaceutical, or food industry, but also to make smart packaging for food or as animal feed [14–18].

The papers published in this Special Issue are briefly described below. They are mainly focused on extraction techniques, in particular green ones, for the isolation and subsequent characterization of bioactive compounds from different matrices, including those commonly considered waste material, thus favoring their recycling and enhancement. In particular, some works report the identification of the bioactive compounds extracted using chromatographic techniques that include traditional detectors, such as UV/Vis, but also more advanced methods, such as Mass Spectrometry and NMR. The final aim concerns the possible use of these compounds for the formulation of functional foods, nutraceuticals, supplements, and cosmetics, but also as a support to pharmacological therapies.

As is known, diabetes is a disease that appears when the body does not produce enough insulin or is unable to use the normal amounts adequately. If not properly controlled, diabetes can cause damage to the kidneys, heart, eyes, and nervous system. In particular, diabetic nephropathy is one of the many complications of diabetes and also represents one of the main reasons why patients undergo dialysis treatments. This pathology, in fact, seriously compromises renal function at the level of the glomeruli. In order to counter these effects, in a work by Basavarajappa et al., the effect of *Coccinia indica* leaf extract was evaluated alone and in combination with pioglitazone, a hypoglycemic drug to modulate progressive kidney damage induced by type 2 diabetes in rats. The results show that *Coccinia indica* leaf extract, a plant already known for its hypoglycemic and antidiabetic properties in the Ayurvedic medical system, with a low dose of pioglitazone, as an antidiabetic therapy, determines a good glycemic control and a beneficial renoprotective effect [19].

Autoimmune diseases share some inflammatory signals, including the secretion of cytokines, which normally play an important role in immune defense. In recent years, the

use of inhibitors to selectively suppress cytokines has opened up new paths of therapeutic exploitation to counteract the symptoms of autoimmune diseases and neoplasms. In this context, several studies have focused on inhibitors of natural origin. Khuranna et al. investigated the optimization of the extraction, quantification, and inhibitory effects of bakuchiol (BKL) cytokines in *Psoralea coryfolia* Linn., a plant that has long been used in traditional Ayurvedic and Chinese medicine. *P. coryfolia* seeds were subjected to different extraction methods, such as maceration, reflux, Soxhlet, and ultrasound-assisted extraction (UAE), and the extracts were quantified using high-performance liquid chromatography (HPLC). An animal model of sepsis induced by lipopolysaccharides (LPS) was used to test the effect of BKL. The results showed that the highest percentage of BKL was present in the extract obtained by the UAE method, which, when administered in animals, was able to decrease the circulating levels of biomarkers [20].

Algae, similar to all plant organisms, are autotrophic, as they produce their own nourishment. Inside them, there may be pigments capable of giving the algae different colors. Osório et al. evaluated the polar and non-polar pigment content of several commercial dried algae. The extraction of the pigments was achieved using different solvents. The results show that the extraction yield depends on the solvent used and the nature of the pigments. Therefore, by appropriately selecting the compound or compounds to be extracted and the most suitable solvents, it is possible to use algae as an important source of pigments for different applications in various sectors [21].

To date, the therapeutic use of *Cannabis sativa* and cannabinoids continues to be debated, although the ability to alleviate the ailments of some serious diseases is recognized, as the scientific evidence is extremely fragmentary and there are no comparable data. In fact, most of the studies have a small number of people and a series of limitations concerning the method of conducting the studies themselves such as, for example, the use of products of different nature, such as sprays, capsules, decoctions, etc., different ways of administration and, therefore, a different absorption in the organism and an unclear description of the long-term effects due to the lack of subsequent controls in most of them. Hence, the importance of conducting further studies on these compounds. In a study by Gallo et al., two methods for the extraction of cannabinoids present in the female inflorescences of *Cannabis sativa* were compared, such as conventional maceration and rapid solid–liquid dynamic extraction (RSLDE). The alcoholic extracts were characterized using high-performance liquid chromatography (HPLC). The results show that although the extraction yield is comparable with the two methods, RSLDE is much faster, with obvious advantages in obtaining bioactive compounds [22].

Several studies have provided information on the composition and nutritional value of the gonads of *Paracentrotus lividus*, an edible Mediterranean sea urchin, while little interest has been reserved for other parts of its body, such as shells and spines, which are generally considered waste material. In a work by Salvatore et al., *P. lividus* shells were extracted by rapid solid–liquid dynamic extraction (RSLDE). Gas chromatography–mass spectrometry (GC–MS) was used to characterize and quantify the fatty acids and their esters contained in the extract. The extract contains arachidonic acid (ARA), 5,8,11,14,17-eicosapentaenoic acid (EPA) and 11-eicosenoic acids and their esters, as well as many polyunsaturated fatty acids (PUFA). These results mean that this extract is of great interest for possible future applications in the medical and/or nutritional field [23].

Zingiber montanum is an important ornamental and medicinal herb of the genus *Zingiber*. Its rhizomes are used in traditional medicine for the treatment of numerous ailments. In a work by Hassan et al., the dried rhizomes were subjected to alcoholic extraction in ethanol. The obtained extracts were analyzed by various column chromatographic methods allowing their characterization. In fact, a sesquiterpenoid derivative, zerumbone, and five derivatives of kaempferol have been isolated, providing useful information on this plant [24].

Another possible candidate in the category of medicinal/food plants is represented by *Lindera neesiana*, a small shrub belonging to the *Lauraceae*, a family of Angiosperms.

The fruits, both fresh and dried, are used as food but also to counteract some ailments. In addition, other parts of the plant, such as leaves, twigs, roots, and bark, also find various applications. Adhikari-Devkota and coll. carried out the hydroalcoholic extraction of leaves and twigs of *L. neesiana*. The chromatographic analysis made it possible to isolate and identify five kaempferol glycosides. In particular, the extract obtained showed a moderate scavenging activity of free radicals and a powerful inhibitory activity of pancreatic lipase [25].

In conclusion, although solid–liquid extraction is a technique that has been known for a long time and which finds application in various sectors, it still has many aspects that require further investigation to fully understand its mechanism of action and to improve the efficiency of extraction. This difficulty is essentially linked to the variety and complexity of the solid matrices to be extracted. Furthermore, there is complete agreement on the part of the scientific community on the need to take care of the sustainability of the analytical procedures, reduce the environmental impact, and favor the recovery of waste. In particular, the recovery of food by-products is a way to reuse the waste from the food chain, recover precious compounds, respect the requirements of a circular economy, and increase the sustainability of the food production system. The development of innovative and sustainable extraction systems for natural products is currently a very topical research topic involving various areas. The goal is to reduce or eliminate the use of hazardous extraction solvents and to ensure a safe and high-quality extract/product in order to protect both the environment and consumers. Therefore, the greatest challenge of research in this area is the identification of the best extraction conditions in order to improve the release of bioactive compounds from the plant waste matrix by reducing the use of solvents and respecting the principles of sustainability of the entire extraction process. Consequently, a sustainable and eco-compatible recovery of bioactive compounds from fruit and vegetable by-products for application in the food, medical, cosmetic, pharmaceutical, or agrochemical industries is essential to increase their added value and reduce the risk of pollution to the environment. Therefore, increasing the number of studies and the development of further lines of research in this direction in the near future can easily be foreseen.

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