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Editorial

Bioactive Compounds from Natural Products: Separation, Characterization, and Applications

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1. Introduction

The study of bioactive compounds represents a new and innovative section of biotechnology, with applications to the well-being of humans. The therapeutic potential of natural health products could be demonstrated by in vitro and/or in vivo biological activities, because the primary aim is to prevent or alleviate different chronic/degenerative diseases. Natural extracts or functional foods (including byproducts) could be valuable substrates through which new products could be obtained. These products display low correlations in in vitro and in vivo activities (antioxidant, anti-inflammatory, or antimicrobial) due to their bioavailability, which is one of their significant limiting factors. The fermentative activities of human microbiota could modulate microbial fingerprints and metabolomic profiles. They alleviate chronic diseases, and their administration could have potent effects (for type 2 diabetes, cardiovascular dysfunctions, or neurodegenerative diseases).

2. Issue Contents

This volume includes eleven research articles and three reviews that vary in their content but all cover research that aimed to characterize the biological effects of natural compounds and the results of quantitative analysis. All of the results displayed are supported by in vitro and in vivo studies or innovative fermentation/extractive processes.

In [1], the authors used *Ulva lactuca* microalgae to extract bioactive compounds with high biological activity. Four solvents were used, of which an ethanol/water mixture (70:30 *v*/*v*) was proven to be the most effective in terms of total carotenoid and phenolic contents. Quantitative analysis was performed using the high-performance liquid chromatography (HPLC) technique. Gallic acid was the predominant phenolic compound, and all-trans-violaxanthin and all-trans-lutein were predominantly identified among the carotenoid compounds. Following in vitro determinations, it was concluded that *U. lactuca* extracts could possibly be used as ingredients in the cosmetic, pharmaceutical, and food industries.

In [2], the authors determined the induction of HL-60 (acute myeloid leukemia cell line) differentiation using biochemical and morphological methods. The data showed that tyrosol (in Maltese Extra Virgin Olive Oil) induces cytotoxicity in HL-60 cells. These data demonstrated that tyrosol is helpful as an adjuvant for differentiating AML models. Upregulated NFkB2 and RELB was displayed after tyrosol treatment, showing this compound's efficacy in reducing inflammatory processes and treating cancer by inducing HL-60 cell apoptosis.

In [3], the anti-inflammatory activity of *Cnidoscolus aconitifolius* was presented using an ethyl acetate extract, and the role of flavonoid content was determined in this study. The anti-inflammatory effect of *C. aconitifolius* extract was determined using the mouse ear edema test induced by the activities of croton oil. The presence of flavonoids was determined using thin-layer chromatography and a spectrophotometric method. The extract resulted in a reduction in induced ear edema at 25–50 mg/kg doses. The results suggest that its use in the treatment of inflammation would be beneficial.

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In [4], hemp oils, isolated from *Cannabis sativa* L., were analyzed using the reverse-phase–high-performance liquid chromatography–photodiode matrix system (RP–UHPLC–PDA) method. A rapid method was developed that can identify and quantify 10 of the most common cannabinoids in *C. sativa* oils: cannabivarin, cannabidiolic acid, cannabigerol acid, cannabigerol, cannabidiol, cannabinol, 9-tetrahydrocannabinol, 8-tetrahydrocannabinol, cannabichromene, and tetrahydrocann. Phytocannabinoid analysis showed which compounds can support the biopharmaceutical use of these products. Such a rapid method has improved the screening of these compounds and helped obtain controlled composition products.

In [5], the authors presented the influence of the drying process on the physicochemical properties of fermented vegetables (beetroot, red pepper, and carrot) in a ratio of 1:1:1 with *Levilactobacillus brevis*, *Lactiplantibacillus plantarum*, and *Limosilactobacillus fermentum*. Two convection drying methods or freeze-drying were used, and the dry matter, color, active substances (betalains and carotenoids), and the bacterial load were determined. Experimental data showed that pomace from fermented vegetables has a vital role in increasing the functional properties of food. Products from dried vegetables can be used in various foods, leading to improved color and an additional supply of probiotic bacteria that ensures the high stability of the products they are incorporated in.

In [6], an ultrasonic enzyme-assisted ATPE (UEAATPE) method was developed to extract flavonoids from the leaves of the *Ficus carica* L. plant which are usually considered waste. UPLC-QTOF-MS/MS was used to identify the flavonoid component, and the significant component identified was quercetin 3-O-hexobioside. The study showed that the recovery of these plant residues could be an essential source of biologically active compounds. In this way, the impact of the accumulation of plant waste on the environment is minimal.

In [7], the use of by-products from yellow onion skins (*Allium cepa* L.) was detailed, mainly by capitalizing on the flavonoid component. Extraction in hot water at 70 °C was performed, and the resulting extract was freeze-dried. Several formulas were extracted before being dried, and an in vitro digestion study demonstrated stability in gastric transit and a controlled release of flavonoid bioactive components during the intestinal phase. The study also showed thermal stability and a controlled pH, indicating that they can be used as functional food ingredients.

In [8], the use of a functional product to inhibit the proliferation of uropathogenic strains of *Escherichia coli* was reported. The product consisted of an ethanolic extract of cranberry fruit (*Vaccinium vitis idaea* L.), St. John's wort aerial parts (*Hypericum perforatum*), thyme aerial parts (*Thymus vulgaris* L.), propolis tincture with 27% dry mass, thyme essential oil, and rosemary essential oil. The tests were performed in a new in vitro bladder simulation system. The in vitro study showed the crucial inhibitory capacity of the proposed product. This initial in vitro study intended to investigate recurrent infections. New functional products were also tested, considering the inhibition of biofilm formation, which was an innovative in vitro research perspective. The system allowed various uropathogenic strains, which are associated with the use of a urinary catheter and participate in the formation of biofilm and the proliferation of inflammatory processes, to be tested.

In [9], the effect of gamma radiation on the mycelium of the fungus *Fomes fomentarius* was presented. A ^{60}Co source was used to induce oxidative stress. The impact on antioxidant stability and total phenol content was determined after 24 h. It was found that 300 Gy was the optimal dose for the extracts in the functional products industry.

In [10], a process for use in the submerged cultivation of the mycelium of the fungus *Inonotus obliquus* was presented to optimize the culture medium to obtain biomass. By analyzing six environmental components and pH, batch bioreactor cultures were performed to confirm the data that was gained from mathematical modeling. This optimized medium had a composition that contained (g/L): malt extract 2.15299, yeast extract 3.99296, fructose 11.0041, soluble starch 17.4, $MgSO_4$ 0.1 g, and $CaCl_2$ 0.05.

In [11], chromatographic and NMR methods described the chemical composition of extracts from callus, cell suspension, and *Rhaponticum carthamoides* roots. Flavonoids, such as ecdysteroids and anthocyanins, can inhibit the proliferation of tumor cells and have other biological effects, which can be used in the future to produce biopharmaceuticals.

In [12], the authors addressed a current health problem: recurrent urinary tract infections and the increasing presence of antibiotic-resistant strains. The paper considered the effect that some less-used plant species have on managing recurrent urinary tract infections. These were pomegranate (*Punica granatum* L.), chokeberry (*Aronia melanocarpa* Michx.), and cornelian cherry (*Cornus mas* L.), and evidence of their potential in the prevention of these infections or as an adjunct to antibiotic therapy was provided.

In [13], the effect of heat treatment on bioactive compounds contained in microalgae was presented as an alternative to increasing the consumption of functional foods. The study showed that there was an increase in oxidative processes, even in the case of short heat treatment times. Phenolic compounds are among the most affected molecules. The effect on the pigments causes discoloration, and the amount of iodine is significantly reduced. The conclusion of this study was that the effect varies from one species to another, and the protein level is also strongly disturbed.

In the last paper [14], aspects related to obtaining an extract from a culture of *Flavobacterium* sp. were presented. The study showed the differences in yield between liquid–liquid extraction using ethyl acetate and liquid–solid extraction using polybenzyl resin. The culture of *Flavobacterium* sp. was isolated from natural products of microbial and plant origin. The effect of pH on the extraction yield was determined. Although both methods isolated the same compounds, differences were identified between the protocols used. These details were considered necessary for various practical aspects.

These articles have demonstrated the potential of using bioactive compounds from natural products in applications associated with human well-being. This Special Issue outlines a broad picture of the study of functional compounds, with many new details on separation, characterization, and biopharmaceutical applications.

These studies have addressed alternative possibilities for preventing and reducing the occurrence of chronic and associated diseases. A new in vitro model has been proposed for the study of recurrent urinary tract infections. The data presented will be a starting point in developing alternative technologies for the extraction of natural compounds but will also serve as an innovative possibility to characterize strategies for the early prevention of infections with antibiotic-resistant strains. The proposal of new sources of functional compounds has been an attractive aspect of capitalizing on lesser-known natural sources.

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