

Editorial

Isolation and Identification of Biologically Active Natural Compounds

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Natural bioactive compounds found in plants, agri-food by-products, microorganisms, marine sources, and other sustainable biological resources continue to drive scientific innovation due to their structural diversity and wide spectrum of biological activities, supporting advances in pharmaceuticals, nutraceuticals, functional foods, cosmetics, agriculture, and animal nutrition [1,2]. Scientific and industrial interest in plant-derived bioactive compounds, including phenolic compounds, polysaccharides, flavonoids, terpenoids, lipids, and other secondary metabolites, is largely attributed to their potential to address current health and sustainability challenges. However, their successful exploitation depends on extraction methodologies that efficiently recover target metabolites from complex biological matrices while maintaining their structural integrity and biological properties.

Although conventional extraction techniques have provided the foundation for natural product research, the growing demand for higher selectivity, sustainability, and analytical performance has stimulated the development of innovative extraction approaches, accompanied by advanced separation and characterization methods [3]. Consequently, the conventional extraction procedures have been increasingly complemented or replaced with greener and more sustainable ones that mitigate the shortcomings of the traditional techniques, including high solvent consumption, low extraction efficiency, and limited selectivity. These emerging technologies improve extraction yields and preserve the integrity of bioactive compounds, while lowering the environmental impact [4]. At the same time, advances in separation science, high-resolution mass spectrometry, and chemometrics are redefining the analytical strategies by moving beyond traditional targeted workflows toward comprehensive chemical characterization of complex natural matrices [5]. Artificial intelligence and machine learning techniques are also reshaping natural products research by enabling predictive modeling, intelligent process optimization, and automated interpretation of complex analytical data.

Despite the progress achieved in recent years, several important challenges remain. The chemical complexity and high variability of natural matrices make standardization and reproducibility difficult to achieve, as they are necessary for more selective, efficient, and sustainable extraction strategies capable of maximizing the recovery of target metabolites while minimizing environmental impact. Furthermore, high-resolution analytical platforms require more robust computational and chemometric tools for the identification of meaningful chemical markers. Another major challenge is to move beyond descriptive phytochemical profiling toward establishing clear relationships between chemical composition, bioavailability, and biological activity through integrated analytical and biological investigations, thereby facilitating the translation of laboratory findings into practical applications across the pharmaceutical, food, cosmetic, and agricultural sectors.



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This Special Issue, *Isolation and Identification of Biologically Active Natural Compounds*, brings together eight original research articles that showcase these emerging research directions. The published contributions cover sustainable extraction technologies, advanced analytical characterization, phytochemical profiling, biological activity assessment, and applications in food science, pharmaceuticals, cosmetics, and animal nutrition. Collectively, they demonstrate how modern separation science integrates extraction optimization, analytical chemistry, and biological evaluation into comprehensive research strategies.

One major topic presented in this Special Issue is the development of sustainable extraction technologies and process optimization. Zhang et al. [6] optimized the subcritical water extraction (SWE) of *Artemisia argyi* leaf polysaccharides using a three-stage hybrid strategy that combines single-factor experiments, response surface methodology (RSM), neural networks (NNs), and a direct search algorithm (DSA). Their study demonstrates how hybrid intelligent optimization algorithms combined with SWE can significantly improve extraction efficiency while supporting environmentally friendly processing. Similarly, Chandrasekaran et al. [7] investigated the ultrasound-assisted extraction of starch and polyphenols from *Canna indica* L. rhizomes, showing how process optimization can increase extraction yields while preserving the functional properties of the recovered compounds. Together, these studies highlight the transition toward environmentally sustainable extraction technologies supported by advanced optimization strategies that maximize both efficiency and product quality.

The second important topic of this Special Issue concerns advanced analytical methodologies for comprehensive chemical characterization of natural products. The phenolic profiles of *Sideritis* species cultivated in Greece were assessed by Kaparakou et al. [8] using an LC-MS/MS-QTOF system. This study highlights the potential of high-resolution mass spectrometry to characterize complex phytochemical mixtures. In a related study, Kokotou [9] applied LC-HRMS for fatty acid profiling in Greek wines. This work demonstrates how advanced analytical techniques enable the characterization of low-abundance lipid constituents that contribute to wine quality and sensory properties. Furthermore, their study highlights the expanding role of separation science in supporting foodomics-oriented research and authenticity studies. Another contribution by Sahlabgi et al. [10] illustrates how comprehensive phytochemical characterization of hydroalcoholic extracts obtained from different parts of *Levisticum officinale* can be successfully integrated with biological evaluation and formulation development. By investigating their incorporation into carbopol-based hydrogels, the authors demonstrate a translational approach that bridges natural product research with pharmaceutical and dermato-cosmetic applications. Collectively, these studies emphasize the important role of modern separation science and high-resolution analytical platforms in generating comprehensive phytochemical knowledge that sustains the development of innovative applications for natural bioactive compounds.

Another emerging topic highlighted by the contributions to this Special Issue is the increasing emphasis on linking chemical composition with biological function. Joo et al. [11] isolated and structurally characterized neuroprotective constituents from *Dryopteris crassirhizoma* rhizomes capable of inhibiting β -amyloid production and BACE1 activity. Their study highlights how advanced separation techniques can be used to identify natural BACE1 inhibitors, which may serve as lead compounds for Alzheimer's disease prevention or therapy. Their work exemplifies the shift from phytochemical identification toward mechanism-oriented biological validation relevant to Alzheimer's disease research. Complementing this perspective, Varzaru et al. [12] investigated the bioaccessibility and biostability of carotenoids, vitamin E isomers, and individual polyphenolic compounds after simulated gastrointestinal digestion of raspberry and blackberry fruits. Their findings emphasize that the nutritional and health-promoting potential of bioactive compounds

depends not only on their abundance in the food matrix but also on their bioaccessibility during digestion, which ultimately determines their bioavailability and biological effectiveness. This work reflects the growing shift in natural product research from describing chemical composition toward understanding the fraction of bioactive compounds that can be effectively utilized by the human body.

The contributions collected in this Special Issue demonstrate the expanding application potential of natural bioactive compounds in pharmaceuticals, functional foods, cosmetics, food quality assessment, and sustainable agriculture. In particular, the investigation of blackthorn and hawthorn fruits by Oancea et al. [13] demonstrates their antioxidant potential and supports their use as alternative feed resources for ruminant nutrition, highlighting their potential to beneficially modulate rumen metabolism and contribute to more sustainable livestock production.

Taken together, the papers included in this Special Issue demonstrate that natural products research is progressively evolving from isolated methodological investigations toward integrated research workflows that combine sustainable extraction technologies, advanced analytical characterization, computational optimization, and biological validation. This convergence of disciplines not only improves our understanding of natural bioactive compounds but also facilitates their translation into practical applications addressing current challenges in healthcare, nutrition, agriculture, and the bioeconomy.

As the field continues to evolve, several research directions deserve particular attention. Despite the significant progress achieved in recent years, important challenges remain in fully exploiting the potential of natural bioactive compounds. The inherent complexity and variability of natural matrices continue to complicate the identification of biologically relevant compounds and the comparison of results across studies, highlighting the need for more robust and integrated analytical strategies. Future research should therefore focus not only on methodological innovation but also on improving the reliability, comparability, and biological relevance of analytical findings through multidisciplinary approaches. AI techniques, including machine learning (ML), deep learning (DL), and cheminformatics, are expected to play an increasingly important role not only in extraction optimization but also in metabolomic data processing, compound annotation, predictive modeling, and biological activity prediction. Furthermore, AI-driven approaches are likely to accelerate bioprospecting and facilitate the discovery and design of novel bioactive molecules [14]. Another promising direction is the increasing integration of high-resolution mass spectrometry with multi-omics approaches. By simultaneously profiling metabolites, lipids, and proteins, MS-based multi-omics provides systems-level insights into the mechanisms underlying the biological activity of natural compounds. Continued advances in MS instrumentation and computational data integration are likely to further enhance biological interpretation and accelerate the discovery of clinically and biologically relevant molecular signatures for precision medicine [15]. At the same time, future studies should place greater emphasis on standardized analytical workflows, bioavailability and *in vivo* validation, mechanistic investigations, and scalable green extraction technologies that facilitate industrial implementation. The continued advancement of green analytical chemistry will remain essential, as it is increasingly recognized not only as a framework for reducing the environmental footprint of analytical processes but also as a key driver of innovation in natural products research and sustainable industrial applications.

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