



Editorial

Polyphenols and Their Impact on Human Health

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Given their potent antioxidant and biological properties [1–3], and in view of their widespread occurrence not only in foods, but also in easily accessible sources such as waste materials from agri-food industries [1,4–6], polyphenols have attracted increasing attention with regard to their possible use as food supplements and as functional ingredients for biomedical and cosmetic applications [7–10].

In this context, the Special Issue "Polyphenols and Their Impact on Human Health" aimed to collect articles reporting innovative applications of natural polyphenols from edible or non-edible sources in the field of nutrition and biomedicine, spanning a range of topics from food supplements or functional foods that prevent oxidative-stress-related diseases to additives in biomedical devices, skincare formulations and cosmetic products. Eight contributions (five research articles and three reviews) have been published in this Special Issue, as listed below:

1. Gravina, C.; Formato, M.; Piccolella, S.; Fiorentino, M.; Stinca, A.; Pacifico, S.; Esposito, A. *Lavandula austroapennina* (Lamiaceae): Getting Insights into Bioactive Polyphenols of a Rare Italian Endemic Vascular Plant. *Int. J. Mol. Sci.* **2023**, *24*, 8038. <https://doi.org/10.3390/ijms24098038>
2. Song, H.; Kang, S.; Yu, Y.; Jung, S.Y.; Park, K.; Kim, S.-M.; Kim, H.-J.; Kim, J.G.; Kim, S.E. In Vitro Anti-Inflammatory and Antioxidant Activities of pH-Responsive Resveratrol-Urocanic Acid Nano-Assemblies. *Int. J. Mol. Sci.* **2023**, *24*, 3843. <https://doi.org/10.3390/ijms24043843>
3. Sánchez-Medina, A.; Redondo-Puente, M.; Dupak, R.; Bravo-Clemente, L.; Goya, L.; Sarriá, B. Colonic Coffee Phenols Metabolites, Dihydrocaffeic, Dihydroferulic, and Hydroxyhippuric Acids Protect Hepatic Cells from TNF- α -Induced Inflammation and Oxidative Stress. *Int. J. Mol. Sci.* **2023**, *24*, 1440. <https://doi.org/10.3390/ijms24021440>
4. Rahn, C.; Bakuradze, T.; Stegmüller, S.; Galan, J.; Niesen, S.; Winterhalter, P.; Richling, E. Polyphenol-Rich Beverage Consumption Affecting Parameters of the Lipid Metabolism in Healthy Subjects. *Int. J. Mol. Sci.* **2023**, *24*, 841. <https://doi.org/10.3390/ijms24010841>
5. Laghezza Masci, V.; Bernini, R.; Villanova, N.; Clemente, M.; Cicaloni, V.; Tinti, L.; Salvini, L.; Taddei, A.R.; Tiezzi, A.; Ovidi, E. In Vitro Anti-Proliferative and Apoptotic Effects of Hydroxytyrosyl Oleate on SH-SY5Y Human Neuroblastoma Cells. *Int. J. Mol. Sci.* **2022**, *23*, 12348. <https://doi.org/10.3390/ijms232012348>
6. Lippolis, T.; Cofano, M.; Caponio, G.R.; De Nunzio, V.; Notarnicola, M. Bioaccessibility and Bioavailability of Diet Polyphenols and Their Modulation of Gut Microbiota. *Int. J. Mol. Sci.* **2023**, *24*, 3813. <https://doi.org/10.3390/ijms24043813>
7. Maisto, M.; Iannuzzo, F.; Novellino, E.; Schiano, E.; Piccolo, V.; Tenore, G.C. Natural Polyphenols for Prevention and Treatment of Urinary Tract Infections. *Int. J. Mol. Sci.* **2023**, *24*, 3277. <https://doi.org/10.3390/ijms24043277>
8. Aleksandrova, S.; Alexova, R.; Dragomanova, S.; Kalfin, R.; Nicoletti, F.; Fagone, P.; Petralia, M.C.; Mangano, K.; Tancheva, L. Preventive and Therapeutic Effects of *Punica granatum* L. Polyphenols in Neurological Conditions. *Int. J. Mol. Sci.* **2023**, *24*, 1856. <https://doi.org/10.3390/ijms24031856>



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Contribution 1 reported preliminary data on the antioxidant and bioactivity, in terms of wound closure ability, of polyphenol-rich extracts from several organs of *Lavandula austroapennina*. Extracts rich in hydroxycinnamoyl derivatives were found to be particularly effective as antioxidants in chemical assays compared to flavonoid-rich extracts, which induced rapid wound closure on HaCaT cells even at low concentrations (1 µg/mL).

Contribution 2 described the preparation, as well as the antioxidant and anti-inflammatory properties, of pH-responsive nanoparticles composed of resveratrol and urocanic acid.

Contribution 3 reported the hepatoprotective effects against inflammation and oxidative stress of the main metabolites of hydroxycinnamic acids; that is, dihydrocaffeic, dihydroferulic, and hydroxyhippuric acids, at concentrations (0.5–10 µM) that are likely to be found in biological compartments after coffee ingestion.

Contribution 4 demonstrated the beneficial effects of a polyphenol-rich beverage containing anthocyanins, flavonoids, chlorogenic acids and ellagitannins with regard to lipid metabolism and DNA integrity in a placebo-controlled human intervention study.

Contribution 5 described hydroxytyrosyl oleate as a promising derivative of the natural phenol hydroxytyrosol, that is endowed with a higher cellular bioavailability. The synthesized compound maintained the anti-proliferative and apoptotic effects of the parent compound at lower concentrations in human neuroblastoma cells.

Contribution 6 explores the interaction of dietary polyphenols, with particular reference to gallic acid, resveratrol, flavonoids and proanthocyanidins, with gut microbiota as an important aspect to be considered when evaluating the health beneficial effects of these compounds. Microencapsulation strategies for improving the positive modulation of gut microbiota induced by polyphenols are also discussed.

Contribution 7 reports the results of in vitro and in vivo studies demonstrating the potential therapeutic efficacy and the mechanism of action of dietary polyphenols (proanthocyanidins, catechins, resveratrol, caffeic acid, and quercetin) against urinary tract infections.

Finally, in contribution 8, the preventive and therapeutic effects, as well as the mechanism of action of phenolic compounds from *Punica granatum* L., mainly ellagitannins, in neurological conditions are reviewed.

The authors of these contributions originate not only from Italy and Spain—countries that are traditionally involved in the scientific research on phenolic compounds, as these compounds are largely responsible for the beneficial effects of the Mediterranean diet—but also from Korea, Germany, Bulgaria, and Slovakia. In addition, the high diversity in the content and scientific approaches presented clearly demonstrates how broad the research field on polyphenols is, and this is even more true considering the topic of the Special Issue was limited to the impact of these compounds on human health.

A fundamental observation emerging from the published papers is that although natural phenolic compounds are intrinsically a source of chemical multifunctionality and may offer unrivalled opportunities as eco-friendly and sustainable compounds, a deep understanding of the structure–property relationships hidden by the complexity of these compounds is crucial to the development of rational strategies for their full exploitation as functional ingredients in the health, food and/or cosmetic sectors.

The collected contributions also help to define the research priorities and underexplored aspects in this field, ranging from the re-evaluation of local, small-scale agricultural products as underexplored sources of polyphenols, the exploration of novel potential applications, and the design of proper formulations or chemical modifications to enhance the biological activity and bioavailability of these compounds, to the evaluation of the role of dietary polyphenol metabolites in the healthy effects of these compounds and the development of in vivo human studies involving not only an extended number but also specific categories of volunteers to develop, for example, new dietary treatments and to obtain more detailed information on the impact of polyphenols on human health.

Conflicts of Interest: The author declare no conflict of interest.

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