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Nutraceutical biodevices from Extra-virgin olive oil and related by-products as innovative and sustainable coatings for biomedical application

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Introduction

So far, Extra virgin olive oil (EVOO) is widely studied for its nutritional and health-promoting properties. A widespread of beneficial effects is attributed to its unique composition, and in particular to polyphenols, bioactive compounds endowed with nutraceutical properties.[1] EVOO production has a great impact in term of sustainability and environment due to the difficult management of the huge amounts of generated by-products such as olive mill wastewater (OMWW) and olive leaves. On the other hand, these discards contain polyphenolic compounds, a valuable source of bioactive compounds to be valorized.[2] Recently, we developed the design of new nutraceutical devices constituted by olive leaf extract (OLE), incorporated in bio-based polymeric scaffolds formed by polyhydroxyalkanoates fibers (PHAs). The obtained OLE/PHA fibers presented anti-inflammatory and immunomodulatory properties, essential in wound healing and tissue regeneration.[3] Starting from these promising results, the purpose of this interdisciplinary project is the valorization of the beneficial properties of EVOO and its related waste OMWW, extending the development of new nutraceutical devices in different biomedical field such as in the treatment of prosthetic infections (PI), the principal complication in prosthetic implant surgery. Nowadays, PI treatment consists in antibiotic therapies, or in the worst cases in a second surgery, affecting copiously the patient's recovery and the healthcare costs.[4] For this reason, the development of an antimicrobial surface containing nutraceutical extracts able to reduce microbial colonization avoiding the common drug-resistance mechanism, might be an adoptable strategy against this infection. Several studies reported EVOO and OMWW as natural antimicrobial agents, due to their polyphenolic composition.[5] Therefore, in this study we aimed to design new biodevices with a potential intrinsic antimicrobial activity, due to the incorporation of EVOO or OMWW extracts in specific biocompatible PHA fibers useful as antimicrobial coating for PI.

Experimental

EVOO and OMWW extracts were characterized by high-performance liquid chromatographic (HPLC) to evaluate their polyphenolic composition. Then the extracts were incorporated using electrospinning technique in PHA fibers and specifically in poly(hydroxybutyrate-co-hydroxyvalerate (PHBHV) fibers. PHBHV is a natural polyester produced by a great variety of microorganisms, presenting high biocompatibility and biodegradability properties.[6] The new EVOO/PHBHV and OMWW/PHBHV fibers were morphologically characterized by Scanning Electron Microscopy (SEM) analysis. The extracts and the new composed nanofibers were evaluated for their antimicrobial activity on representative PI bacteria (Gram + (*Staphylococcus epiedrmidis)* and Gram – (*Pseudomonas*

aeruginosa)) by Agar Gel Immunodiffusion assay (*Halo test*). In order to investigate the release of phenols from the polymer, the diffusion of the main phenolic compounds in PBS buffer was determined at defined time intervals by HPLC analysis. Moreover, Almar blue assay was performed to evaluate the cytocompatibility of the new biofibers.

Results and Discussion

The evaluation of polyphenolic composition of EVOO and OMWW extracts revealed the high presence of important polyphenols presenting antioxidant and antimicrobial properties, such as hydroxytyrosol, tyrosol and pinoresinol, being natural sources of antimicrobials. In fact, both OMWW and EVOO extracts revealed a good inhibition of bacteria growth. The obtained composite nanofibers (EVOO/PHBHV and OMWW/PHBHV) presented uniform size (about 1-2 µm diameter) and a reproducible morphology. The EVOO/PHVBH fibers maintained the antimicrobial effect, showing an improved cytocompatibility compared with the singular EVOO extracts and a gradual and complete release of polyphenols in 48 h. Studies on the antimicrobial properties of OMWW/PHVBH fibers are ongoing.

Conclusions

EVOO and OMWW extracts demonstrated promising antibacterial properties thanks to their polyphenolic composition and were incorporated on specific PHVBH nanofibers for the development of new nutraceutical devices. These new biodevices might be useful as antimicrobial coating for biomedical application and in particular to contrast PI. The project well aligns with the sustainable purposes of Recovery and Resilience Plan (PNRR), concerning the revalorization of food waste supply chain using a sustainable and biocompatible coatings.

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Biography

Doretta Cuffaro has completed PhD in “Drug science and Bioactive substances” at University in Pisa in 2018. During the PhD she was visiting PhD student at University of Oxford (UK), developing biological screening cell based assays. The PhD and the post-doc research were spent on the design and synthesis of proteinase inhibitors. Since February 2022 she is type A fixed-term researcher at the Department of Pharmacy of the University of Pisa. Her research mainly focuses on the study of nutraceutical properties of bioactive compounds presented in food and in the wastes deriving from food supply chain. She is co-author of 29 papers in peer-reviewed journal, and 1 patent.

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