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Introduction

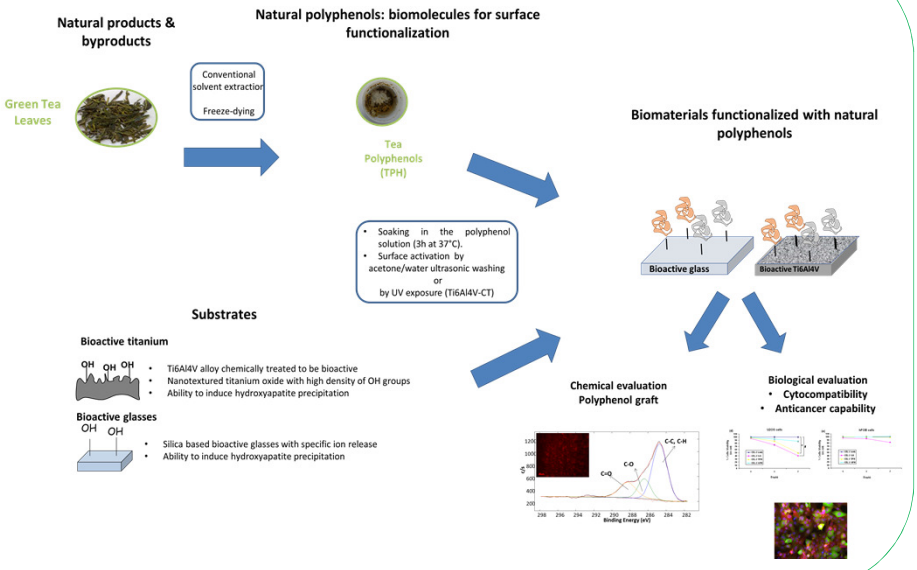
Polyphenols are a structural class of natural-derived compounds characterized by the presence of multiples phenol groups. Each polyphenol has specific biological properties depending on the number and characteristics of phenol structures.

In the last few decades polyphenols have been intensively studied because of their supposed capability to modulate inflammatory response to prevent cancerization and to promote tissue regeneration[1] and recently they have been suggested to functionalize the surface of currently used biomaterials to improve the final medical devices performance.

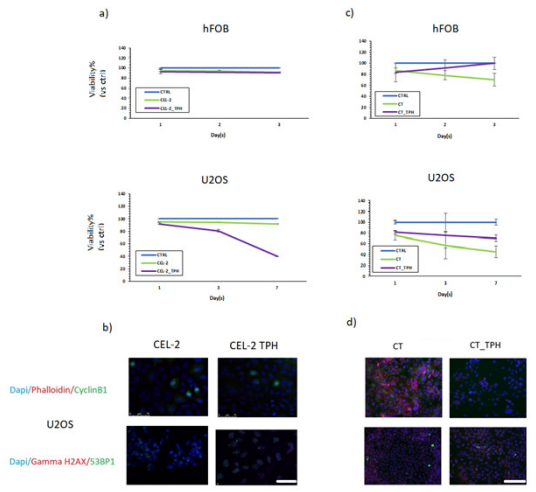
The aim of the present work was to couple natural polyphenols extracted from green tea leaves to the surfaces of Ti6Al4V alloy and bioactive glass to promote functionality in healthy bone cells and death induced by DNA damage in cancer cells.

Material and methods

Bioactive glass (CEL2) has been prepared by melt and quenching technique[2] while Ti6Al4V has been chemically treated (Ti CT) to obtain an oxide surface with nanotextured morphology enriched by hydroxyls groups[3]. Polyphenols were extracted from green tea leaves (TPH) by solvent extraction, freeze-dried, resuspended in water and used to soak activated substrates. Finally, surfaces' coating was chemically activated by UV exposure. Surface analysis was performed by means of Folin&Ciocalteu test, XPS and fluorescence analyses. Polyphenols selective antitumoral activity was investigated on human osteosarcoma derived osteoblasts (U2OS) in comparison with non-tumorigenic progenitor (human- fetal derived osteoblasts – hFOB) by means of viability assay. The DNA damage and repair were evaluated by nuclear immunolocalization of 53BP1 and cyclin B1.



RESULTS AND DISCUSSION



The photometric Folin&Ciocalteu tests based on redox reactivity demonstrated the effective grafting of bioactive and redox-active polyphenols, while XPS and fluorescence analysis revealed the presence of unmasked functional groups.

Despite those preliminary results, polyphenol capability to selectively affect cancer cells was appreciable only in coated bioglasses.

As shown in figure 2a, the viability of bone cancer cell line (U2OS) was significantly affected in comparison with hFOB cells. Moreover, tumorigenic U2OS cells cytology revealed the presence of DNA-damage foci established by 53BP1 analysis. Nuclear localization of cyclin B1 confirmed that the DNA-damage cannot be repaired (figure 2b).

On the contrary, despite an initial TPH induced cytotoxicity of U2OS, cancer cells viability increased during the analysis reaching controls value (figure 2c). Additionally, the DNA damage and repair assay didn't show irreversible DNA damage for U2OS cells growth on coated TiCT (figure 2d)

CONCLUSIONS

Natural-derived polyphenols were successfully grafted onto bioactive glass surfaces without losing polyphenol capability. In particular, polyphenols were able to selectively reduce cancer cells viability via ROS/RONS mediated DNA-damage and to preserve the viability and proliferation rate and of healthy osteoblastic progenitor cells.

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