Novel antioxidant catechols: biosynthesis, characterization and biological activity

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Catechols are ubiquitous in nature and are extensively used in the chemical and pharmaceutical industries (Lekseet al., 2001; Schweigert et al., 2001). These compounds, as well as their substituted derivatives, are very susceptible to oxidation and react quickly with various oxidizing agents, including free radicals. Thus, catechols may act as antioxidants in human cells, preventing degenerative diseases caused by free radicals, such as cancer, heart disease and immune system decline (Cavalier et al., 2001). Much attention has been recently dedicated to the synthesis and characterization of novel catechols to study, among others, how the different nature of the substituents bound to the catechol ring may influence the reactivity towards oxidizing agents, the pharmacokinetics, the tissue and cellular distribution of these compounds. However, the synthesis of substituted catechols by chemical methods is often complex and may involve severe reaction conditions, resulting in low yields and the formation of racemic mixtures. Bacterial Multicomponent Monooxygenases (BMMs), both as purified enzymes or expressed as whole cells biocatalysts, have several attractive properties which make them privileged catalysts for oxyfunctionalization reactions on aromatic compounds such as benzenes and phenols to produce the corresponding catechols. In this work we have investigated the use of a BMM, the ToMO complex from *Pseudomonas* sp. OX1 expressed recombinantly in *E. coli* strain JM109, to hydroxylate non-natural, commercially available aromatic compounds to produce novel antioxidant catechols (Notomista et al., 2011). The starting aromatic compounds used in this bioconversion were: 2-phenoxyethanol, 2,3-dihydrobenzofuran, and 2-indanol.
Catechols obtained from the hydroxylation of these compounds were purified on HPLC and identified by NMR and mass spectrometry analysis. Their antioxidant potential was first assessed by using the DPPH chemical assay; the antioxidant efficiency obtained was in all cases comparable to that of hydroxytyrosol, a strong antioxidant catechol present in extra-virgin olive oil (Alagna et al., 2012). All catechols were then tested on cardiomyoblast cell line H9C2 following two distinct procedures: a) evaluation of possible toxic effects (e.g. cell viability and apoptosis); b) evaluation of their protective effect during oxidative stress induced by sodium arsenite (e.g. analysis of stress granules by confocal immunofluorescence). MTT and EB/AO (ethidium bromide/acridine orange staining) assays showed no effects on viability and apoptosis, respectively. Conversely, pretreatment with cathecols of cardiomyoblast cells, where oxidative stress was induced with sodium arsenite, resulted in a significantly lower percentage of cells containing granules as well as lower density of stress granules. Catechols treatment, however, did not affect the process of stress granule maturation.

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