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## Molecular and cellular targets of polyphenols from Fragaria vesca leaf

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Natural products have been a fertile source of novel lead molecules for drug discovery, being for long known that many plantderived compounds have anti-inflammatory, antioxidant and anticancer activities. *Fragaria vesca* has been used by traditional medicine for the treatment of several diseases. In order to validate and evaluate the mechanisms involved in the activities previously reported, a hydroalcoholic extract from *Fragaria vesca* leaves was obtained. Using a mouse macrophage cell line we observed that the extract inhibited the production of nitric oxide (NO) triggered by lipopolysaccharide, partially due to a direct scavenging of NO. The extract also affected the cellular proteolytic pathways, through the reduction of proteasome activity and modulation of autophagic machinery, mechanisms that are therapeutic targets in cancer treatment. In order to identify the compounds responsible for these effects, the extract was further fractionated and the different fractions screened in human hepatocellular carcinoma cells (HepG2). The ellagitannin-enriched fraction (EEF) had the lower IC50 for cell viability and was then selected to pursuit the study. EEF induced cell cycle arrest at G2/M checkpoint, decreased cell proliferation and inhibited both autophagy and ubiquitin-proteasome system. Furthermore, to study the cytotoxic mechanism of EEF, an iTRAQ (isobaric tag for relative and absolute quantitation) based proteomics approach was used. Several proteins (914) were identified, among which 133 were significantly modulated, most of them related to metabolic processes. Overall, EEF decreases cell proliferation through different mechanisms involving diverse molecular targets, suggesting that *Fragaria vesca* could be a source of valuable molecules with anticancer potential.

## Biography

Joana Liberal completed her master degree in Molecular and Cell Biology in 2008 at University of Aveiro, and is currently finishing her PhD work, in Pharmacognosy and Molecular Biology fields, at Center for Neuroscience and Cell Biology of University of Coimbra. Her research interests are focused in the evaluation of the biological properties of natural products and the underlying molecular mechanisms. She has published 10 papers to date, one provisional patent application and one book chapter.

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