

Plant-derived polyphenols and intestinal HT-29 cells: understanding the cellular uptake

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Research in recent years strongly supports a role for polyphenols in the prevention of chronic and degenerative diseases, particularly cancers, cardiovascular and neurodegenerative diseases. A large number of epidemiological studies have shown that a diet rich in polyphenols may have a role in the prevention of atherosclerosis and diabetes vascular complications.

The polyphenols have aroused great scientific interest, since their beneficial effects are attributed to their antioxidant activity: the phenolic compounds can act as metal chelators and radical scavengers, and might also trigger changes in cells and in the signaling pathways, as by preventing the LDL oxidation, platelet aggregation, and ROS generation. The health effects of polyphenols depend also on their bioavailability, which can vary greatly because of different factors, as the degree of hydroxylation, the molecular conformation, etc. A critical point in the debate on health effects of polyphenols is indeed their bioavailability, therefore we used the human colorectal carcinoma cells (HT-29), which are a reference model of intestinal cells, to evaluate the polyphenols ability to pass through the cellular membrane and permeate into the cell.

The polyphenols studied in this research are from medicinal plants widely used in traditional medicine: baicalein (from *Scutellaria baicalensis* G.), eupatorin (*Eupatorium semiserratum* DC.), galangin (*Alpinia officinarum* L.), magnolol (*Magnolia officinalis* L.), myricetin (*Myrica rubra* S. Z.), oleuropein (*Olea europaea* L.) and silybin (*Silybum marianum* L.).

To assess the cellular uptake of polyphenols, we incubate the HT-29 cells for three hours with each flavonoid compound at 5 μ M. At first, we assessed the polyphenols stability in the culture medium (HBSS), then we analyzed the extracellular and intracellular content by high performance liquid chromatography (HPLC) equipped with a UV diode array detector.

The results showed that the flavonoids baicalein, eupatorin and galangin are able to pass through the HT-29 cell membrane and can also undergo biotransformation process; among others, baicalein has been taken up in the cells during the three hours, in this time it has also been transformed in different metabolites. The major metabolite has been identified as baicalein-7-glucuronide ($0,60 \pm 0,20$ nmol/mg_{prot}), the conjugated form of baicalein after phase-II metabolism. Conversely, oleuropein seemed to not been taken up in the HT-29 cells, since after the three hours it was found in the extracellular solution at the concentration of $4,81 \pm 0,54$ μ M.

These results gave new information about the polyphenols ability to permeate the intestinal HT-29 cells, and suggest that the flavonoids, which are able to pass through the cellular membrane, can act as scavenger of reactive oxygen species inside the HT-29 cells and be effective antioxidant agents. Further studies are needed to deepen the research on the cellular permeability of these natural compounds.