

POST-DOC PLAN

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TITLE: Biomarkers of the intake of dietary polyphenol using metabolomic approach

Abstract

Diets rich in fruit and vegetables are usually associated with health and a reduced risk of developing several diseases such as cardiovascular diseases and many forms of cancer. In fact, these healthy effects have been related to the phytochemical (mainly polyphenol compounds) of plants and/or plant-derived foods. Initially, the biological activity of the dietary vegetable and fruits polyphenols were attributed to their strong antioxidant capacity, but investigations into the mechanism of action has demonstrated to be more complex, involving modulation of the gene expression and cellular signaling processes. Another important challenge related to the characterization of the biological action of polyphenols, such as flavonoids, refers to the very limited current knowledge regarding their bioavailability, mainly the role of the polyphenol metabolism. Metabolomics has been proposed as a powerful tool to explore the complex relationship between nutrition and metabolism, since it studies the modifications in the metabolome (the set of metabolites present in a cell, tissues or biological fluid) under the effect of genetic and/or physiological or environmental factors. Thus, the goals of this work are, initially, the characterization of the polyphenol in Brazilian typical fruits, identifying new sources of fruits with potential biological activity. Furthermore, develop and apply metabolomics tools in clinical studies using healthy and/or non-healthy volunteers in order to evaluate the impact of the polyphenol intake on the overall metabolism. One important challenge in nutritional metabolomics is identify new biomarkers or biomarker patterns that could be use to estimate the dietary phytochemicals consumption or exposure and new markers of effects in order to correlate the intake of phytochemicals with health effects *in vivo*.

Work plain

Firstly, the goal of the project is the characterization of Brazilian fruits, considering content and chemical structural identification of polyphenol, mainly flavonoids. These compounds will be separated and quantified by HPLC-DAD and characterized by HPLC-ESI-MS/MS according to the methods already used in our group (Hassimotto et al., 2008). Also, the fruits extracts will be evaluated, using *in vitro* models, regarding their antioxidant activity (ORAC and DPPH methods), antiinflammatory properties (macrophage cell culture) and antihypertension activity (HPLC method). The fruits or fruit pulps will be select according

their commercial and season availability. The data generated *in vitro* models will provide, together with the compositional data, indications about the potential of food, as well as their phenolic compounds, on health promoting and reducing the risk of chronic diseases development.

In the second phase of the project, metabolomics approach will be used to characterize the intake and change in endogenous metabolic profile, allowing the identification of direct or indirect markers of their intake. Polyphenol metabolism may produce several classes of metabolites that could become a robust new biomarker of polyphenol intake. Firstly, the vegetable extract or food of the selected sources of polyphenols will be administered, in a single dose, to healthy and/or non healthy volunteers. The urine samples were collected before and after intake (24-h urine samples) and analyzed by liquid chromatography-mass spectrometry (LC-MS/MS) and multivariate statistical analysis (PCA). Plasma also will be collected in a time to be determined. Knowledge of the pharmacokinetic and the properties of the flavonoids could be useful to identify possible biological activity without a restriction of a metabolic pathway or of specific disease pattern. Moreover, the identification of the specific biomarkers of intake is important to estimate the flavonoid exposure from diet or to estimate the exposure by dietary assessment.

References

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Chronogram

Activities	Year 1	Year 2
Bibliographic research update	x	x
Characterization and identification, by HPLC-DAD-MS/MS, of the phenolic compounds in the fruit extracts	x	
Determination of the biological activity in vitro models	x	
Developing and application of metabolomic approach in biological fluids, after fruit extract intake	x	x
Preparation of reports	x	x