Olanzapine-induced steatosis in and mitochondrial dysfunction are inhibited by dietary anthocyanins

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Introduction: Second-generation antipsychotics (SGAs) are the cornerstone of therapeutic guidelines for psychotic disorders worldwide. "Off-label" applications of SGAs include now millions of non-schizophrenic adults and children. The SGAs users develop insulin resistance and hepatic steatosis alterations shortly after initiation of the pharmacotherapy. Among other mechanisms, SGAs induce dysfunctions of hypothalamic satiety centers, increase peripheral lipid accumulation and the up regulation of the sterol regulatory element-binding protein 1c (SREBP1c). In this work, we show pre-clinical evidence on the protective effect of dietary anthocyanins from the Chilean blackberry, known as MaquiBerry, against the weight gain, lipid accumulation in human HepG2 hepatocytes, SREBP1c gene expression, and mitochondrial dysfunction induced by the antipsychotic drug olanzapine (OLZ).

Methods: Cultured human HepG2 hepatocytes were treated with OLZ to induce lipid accumulation and SREBP1c gene expression. The OLZ-induced intracellular lipid accumulation was verified by Nile Red fluorescence and Oil Red staining, intracellular cholesterol and triglycerides were measured by standard colorimetric methods. Gene expression of the transcriptional factor SREBP1c was measured by q-PCR. Dietary anthocyanins from Maqui berry (MANT) at dose of 73 mg/Kg for 21 days were fed to Sprague-Dawley rats treated with OLZ (4mg/kg i.p.). Rats were then evaluated for weight gain and plasma triglycerides levels.

Results & Discussion: OLZ-induced intracellular lipid accumulation in HepG2 cells was significantly inhibited by Maqui anthocyanins. The OLZ-induced triglyceride and cholesterol synthesis was also inhibited by MANT. OLZ-induced weight gain in Sprague-Dawley rats was also inhibited by MANT. Delphinine-3-glucoside (major component of MANT) protected HepG2 cells from OLZ-induced lipid accumulation and prevented OLZ-induced mitochondrial dysfunction in L6 skeletal muscle cells.

Biography
Rojo L E is registered Pharmacist in Chile and has a Doctoral degree in Pharmacology from the University of Chile. His Doctoral thesis was done at the University of Chile and at the Albert Einstein College of Medicine in New York, USA. He has joined the group of Dr. Ilya Raskin at the School of Biological and Environmental Sciences at Rutgers University as a Postdoctoral Associate and now, he is an Associate Professor of Toxicology at Universidad de Santiago de Chile.

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