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NATIVE PLANTS AND NEUROPROTECTIVE EFFECTS IN DIABETES MELLITUS

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In Cuyo region (Argentina) Tessaria absinthioides (Ta) and Oxalis erythrohiza (Oe) are popularly consumed to regulate glucose (Glu) and cholesterol (Chol) levels, lacking of scientific support. Several works indicate that 85% of world population uses "medicinal plants" to treat its health. Diabetes mellitus patients have chronic hyperglycemia, oxidative stress state and can also develop neurodegenerative changes. This is a problem for health systems, thus the search of alternative therapies remains in force. Previously, we had shown effects of Ta and Oe decoctions (10% W/V) on metabolism and LXR expression in hypothalamus (HT). In this work, adult male rats (SD), controls (C, i.p.veh.) or diabetics (D, i.p. STZ 30 mg/Kg) drink decoctions (10% W/V) of Ta (CTa/DTa), Oe (COe/DOe) or water (CW/DW) by 4 weeks. Glu, Chol and triglycerides (TG) levels were measured on blood samples by commercial kits. Neural NOS (nNOS) and Neurofilaments bands were higher in DW and COe+/Ta+ than CW (28%; 14% and 19% resp.; p<0.05). However, the value of NF200 in DTa were lower than DW (25%; p<0.05) and closer to CW. In DW and COe the nNOS were higher than in CW (43% and 70% resp.; p<0.05), however the decoctions had not effect on D. Results suggest that these plants could have metabolic and neuroprotective effects. A more extended treatment will be necessary to propose Oe and Ta like new therapeutic tools (PPP043,PIO-SECTIT2250, CICITCA UNSJ, CONICET).

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EFFECT OF THE PROINFLAMMATORY MICROENVIRONMENT ON HUMAN DOPAMINERGIC PRECURSORS SURVIVAL AND DIFFERENTIATION

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Parkinson ´s Disease (PD) is a neurodegenerative disorder characterized by the loss of dopaminergic (DA) neurons of the substantia nigra pars compacta. Successful transplantation of dopamine-producing cells into the striatum has been shown in animal models and clinical trials. However, beneficial effects are constrained because of the remaining low number of DA neurons grafted. This could be due to host inflammatory response, among other factors. Few reports have addressed the issue of inflammatory response on the survival and differentiation of the transplanted cells. We studied the host primary response related to the graft of human DA precursors (DA14) in vivo and the impact of proinflammatory factors on the viability and differentiation process of DA14 cells in vitro. Our in vivo resultsshowed a significant increase (P<0.05) of host-MHCII and GFAP positive cells associated to the human graft after 15 days post-transplant of DA14 cells into immunosuppressed rats. To study the effect of microglial activation, BV2 microglial cells were treated with LPS, and nitrite and TNF alpha production were determined. DA14 cells were exposed to conditioned media (CM) from basal and activated BV2 cells during 4 days and immunofluorescence (IF) for Tyrosine hydroxylase (TH) (DA neuronal marker) was performed at DA28 stage. Results from TH cell counting revealed that DA14 incubated with CM from activated microglia significantly decreased the number of DA neurons at DA28 (p<0.05). In order to study the short term effect of inflammatory environment, DA14 cells were then exposed toCM from basal and activated BV2 cells during 4 days. After this treatment differentiation and survival assays were performed. TH cell counting suggested that CM from activated microglia during 4 days significantly decreased the number of DA cells (p<0.05). During this period of time, Hoechst staining showethed the inflammatory factors from activated microglia significantly increasedcell death (p<0.05). DA cell morphology analysis was performed to evaluate the differentiation process. Decrease in the percentage of neuronal morphology-like cells was conveyed by neurite length alterations after 4 days with CM activated microglia. In this proinflammatory context, we also observed a negative modulation of two transcription factors involved in dopaminergic differentiation: Foxa-2 and Nurr-1. Altogether our findings suggest that, microglial cells could play a fundamental role in the survival and differentiation of DA precursors. The cellular and molecular mechanisms involved in these processes should be considered and deeply analysed to improve cell replacement therapy.