NEUROPROTECTIVE EFFECTS INDUCED BY *BACOPA MONNIERI* AGAINST METHAMPHETAMINE AND MPP+ TOXICITY IN CATECHOLAMINE CELLS *IN VITRO*

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Methamphetamine (METH) and 1-methyl-4-phenylpyridinium (MPP+) are neurotoxins, which damage catecholamine neurons with substantial differences in their molecular and cellular mechanisms. In fact, while METH neurotoxicity mostly depends on oxidative species, MPP+ toxicity depends on the inhibition of mitochondrial activity. This explains why only a few compounds protect against both neurotoxins. Recently, evidence shows that phytochemicals may protect against neurodegeneration. This involves counteraction oxidative stress. Therefore in the present study we investigated whether: (i) natural extracts from *Bacopa Monnieri* (BM) may protect both METH and MPP+ toxicity; (ii) protection occurs along with suppression of reactive oxygen species (ROS); (iii) BM prevents mitochondrial alterations. The protective effects were measured in catecholamine cells by light and electron microscopy, with MitoTracker Red and Green as well as by ultrastructural morphometry of mitochondria. We found that BM dose-dependently protects against mitochondrial damage by suppressing mitochondrial crest destruction and matrix dilution and by increasing the amount of healthy and total mitochondria. This effect is related to the reduction of ROS formation. The present data provide evidence that BM protects catecholamine cells by exerting a powerful antioxidant action and preserving mitochondrial integrity, independently by the type of experimental toxicity.

ADIPOSE STEM CELLS FOR BLOOD-RETINAL BARRIER REPAIR

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In the last few decades, adipose-derived mesenchymal stem cells (ASCs) have been widely investigated in the field of regenerative medicine because of their multipotent differentiation ability. In fact, they can give rise not only to elements of mesodermal origin, but also to elements of different cell lines such as neurons or glial cells. In the present work, we tested a pericyte (PC) differentiation of ASCs in order to provide a tool to overcome the massive PC loss occurring in cases of diabetic retinopathy, characterized by the blood-retinal barrier (BRB) impairment due to altered interactions between endothelial cells and PCs. To this aim, pericyte-like ASCs (P-ASCs) were obtained by growing them in a specific PC medium. In addition, some samples of P-ASCs were cultured in high glucose (HG) conditions to mimic the altered microenvironment of a diabetic eye. Their possible beneficial effects were assessed in co-cultures of P-ASCs and human retinal endothelial cells (HRECs). Results obtained by immunofluorescence techniques show that, compared to native ASCs, the presence of P-ASCs induced an increased endothelial expression of junction proteins (VE-cadherin and ZO-1), suggesting an improved BRB integrity, as also indicated by higher values of trans-endothelial electrical resistance. Moreover, by three-dimensional co-cultures carried out in Matrigel, it was possible to demonstrate that P-ASCs were preferentially positioned in the same location as native PCs, i.e. around the typical tubular, vessel-like structures formed by HRECs. It can be concluded that P-ASCs may represent a valuable tool to develop therapeutic strategies to counteract BRB disruption in case of diabetic retinopathy.

THIOCTIC ACID AND CDP-CHOLINE MODULATE THE NEUROINFLAMMATION IN LPS-STIMULATED MICROGLIA CELLS AND HIPPOCAMPUS OF HYPERTENSIVE RATS

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Brain diseases may occur as a consequence of neuroinflammatory cascades, including alterations in the cross-talks between glial cells and neurons due to the activation of microglia and astrocytes. The aim of the study was to investigate whether (+)-thioctic acid (TIO) and CDP-choline (CDP) alone or in association could block the inflammatory response in lipopolysaccharide (LPS)-stimulated BV2 microglia cells and in the hippocampus of 24-week-old spontaneously hypertensive rats (SHR). A murine microglial cell line was incubated with LPS and different concentrations of both compounds for 24 h. Following treatments, the cell viability assay did not show significant changes. LPS promoted morphological alterations, an increase in ionized calcium-binding adapter molecule 1, and interleukin-1 beta levels accompanied by nuclear translocation of nuclear factor-kappa B. These changes were reversed after the treatments with both TIO and CDP. The results of *in vitro* experiments were consistent with those obtained in the hippocampus of SHR rats treated for four weeks with TIO and CDP, alone or in combination. On the other hand, treatment with TIO and CDP attenuated gliosis and microglial activation. Moreover, the expression levels of interleukin-1 beta and nuclear factor-kappa B were decreased. These findings suggest that the use of an antioxidant compound associated with a cholinergic neurotransmission enhancer could represent an approach for treating brain disorders characterized by neuroinflammation and vascular impairment.