

Effect of acute administration of dietary *Pistacia lentiscus* L. essential oil on the ischemia-reperfusion-induced changes in rat frontal cortex and plasma

Serra M.P.¹, Quartu M.¹, Boi M.¹, Pillolla G.², Melis T.¹, Poddighe L.¹, Del Fiacco M.¹, D. Falconieri³, Carta G.^{4,5}, Piras A.^{4,5}, Murru E.^{4,5}, Collu M.², Banni S.^{4,5}

¹ Dept Cytomorphology, Univ. Cagliari, Monserrato, Italy

² B.B. Brodie Dept Neuroscience, Univ. Cagliari, Monserrato, Italy

³ Dept of Chemical Sciences, Univ. Cagliari, Monserrato, Italy

⁴ Dept Experimental Biology, Univ. Cagliari, Monserrato, Italy

⁵ Nutriscience, srl, Pula, Italy

In this study *Pistacia lentiscus* L. essential oil (E.O.), a mixture of terpenes and sesquiterpenes, was tested for its protective effects in cerebral ischemia/reperfusion-induced injury in Wistar rat frontal cortex and plasma. Cerebral ischemia was produced by a 20 min bilateral common carotid artery occlusion followed by 30 min reperfusion. *Pistacia lentiscus* L. essential oil (E.O.) (200 mg/0, 45 ml of sunflower oil as vehicle) was administered via gavage 6 hours prior to ischemia. Rats were randomly assigned to four groups, ischemic/reperfused (I/R) and sham-operated rats treated with the vehicle or with E.O.. Different brain areas were analysed for fatty acid changes and expression of the enzyme cyclooxygenase-2 (COX-2). Ischemia/reperfusion triggered in frontal cortex a decrease of docosahexaenoic acid (DHA), the membrane highly polyunsaturated fatty acid (HPUFA) most susceptible to oxidation. Pre-treatment with E.O. prevented this change and led further to decreased levels of COX-2, as assessed by Western Blot. In plasma of ischemic/reperfused rats, E.O. administration increased both the DHA-to-eicosapentaenoic acid (EPA) ratio and levels of the endocannabinoid congeners palmitoylethanolamide (PEA) and oleoylethanolamide (OEA).

The results obtained suggest that ischemia/reperfusion triggers a cerebral insult sufficient to cause a region specific lipid peroxidation as evidenced by the detectable, significant decrease in the tissue level of DHA, the most abundant essential fatty acid of neuronal membrane phospholipids. Acute dietary pre-treatment with E.O. triggers modifications both in the frontal cortex, where COX-2 expression decreases and the decrease of DHA is apparently prevented, and in plasma, where PEA and OEA levels increase. We suggest that the activity of PEA and OEA, as endogenous ligands of the peroxisome proliferator-activated receptor (PPAR)-alpha, by inducing the peroxisomal beta oxidation, may explain the observed increase in the DHA/EPA ratio. The latter, in fact, might account for an increased metabolism of n-3 aimed at restoring DHA within damaged brain tissue. The possibility that changes in fatty acid metabolism and plasmatic availability of PEA and OEA are correlated events represents an issue worth future investigations.

Keywords: Cerebral ischemia/reperfusion, DHA, COX-2, PEA, OEA, *Pistacia lentiscus* L.