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Oxidative stress (OS), involved in the pathophysiology of male infertility, results in sperm membrane peroxidation (LPO).

I tested *in vitro* the antioxidant effect of *C. sativa* leaf extract upon ejaculated human sperm. Different dilutions of this extract were used to test the toxicity on sperm motility. LPO was induced by 100µM H<sub>2</sub>O<sub>2</sub> and evaluated by the levels of malondhyaldehyde (MDA), a marker of LPO. The extract was tested in *swim up* selected sperm incubated with H<sub>2</sub>O<sub>2</sub> alone and with H<sub>2</sub>O<sub>2</sub>+extract (1:200), sperm morphology was analyzed by transmission electron microscopy (TEM). The extract did not decrease sperm motility but reduced MDA levels suggesting an antioxidant/protective effect at plasma membrane level as detected by TEM analysis.

I carried out clinical studies in groups of patients with pathologies related to infertility involving OS (leucocytospermia, varicocele, idiopathic infertility) and fertile men. Sperm parameters were evaluated according to WHO (2010) and by mathematically elaborated TEM analysis providing a fertility index and percentages of sperm immaturity, necrosis and apoptosis. F<sub>2</sub>-isoprostanes (F<sub>2</sub>-IsoPs), produced by non-enzymatic metabolism of arachidonic acid, F<sub>2</sub>-dihomo-isoprostanes (F<sub>2</sub>-dihomo-IsoPs) from adrenic acid and F<sub>4</sub>-neuroprostanes (F<sub>4</sub>-NeuroPs) from docosahexaenoic acid were considered as LPO indices. Our results suggested an involvement of isoprostanes in male infertility. F<sub>2</sub>-IsoP and F<sub>2</sub>-dihomo-IsoP levels increased in varicocele group, F<sub>2</sub>-IsoPs positively correlated with immaturity and F<sub>4</sub>-NeuroPs negatively with normal morphology. In idiopathic infertile men, F<sub>4</sub>-NeuroPs positively correlated with necrosis.

Phospholipase A<sub>2</sub> (PLA<sub>2</sub>) releases the F<sub>2</sub>-IsoPs in semen in a free form. PLA<sub>2</sub> levels were detected in semen of fertile and infertile men by immunological method. PLA<sub>2</sub> was increased in varicocele and showed negative correlation with normal morphology. These data confirm the involvement of isoprostanes pathway in sperm infertility.

**Publications:**

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3. Biagi M, Noto D, Corsini M, Baini G, Cerretani D, Cappellucci G, Moretti E. *Antioxidant Effect of the Castanea sativa Mill. Leaf Extract on Oxidative Stress Induced upon Human Spermatozoa*. Oxid Med Cell Longev. 2019 Dec 19;2019:8926075.
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