# ESTROGENES ALLEVIATE MITOCHONDRIAL DYSFUNCTION IN THE HEART OF OVARIECTOMISED RATS WITH METABOLIC SYNDROME

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**Introduction.** It is believed that premenopausal females have a reduced incidence of cardiovascular disease. Much of this protection is attributed to beneficial effects of estrogen on the lipid profile and endothelial cell function, but recent data have suggested that estrogen also can protect cardiomyocytes and mitochondria are a major target of cardioprotective signaling.

**Aim**. To assess the effects of 17β-estradiol ($E_2$) on mitochondrial respiratory chain activity and oxidative status in the heart of ovariectomised rats with fructose-induced insulin resistance.

**Materials and methods.** Female Wistar rats were divided into four groups: control intact rats (C, n=8), ovariectomised rats fed on a regular diet (OVX, n=8), OVX rats which had free access to 250 g/L solutions of fructose for 8 weeks (OVX+HFD, n=8), and OVX rats treated with $E_2$ (20 μg/kg/day per os) during 2 months of HFD feeding (OVX+HFD+$E_2$). Mitochondria were isolated by differential centrifugation from the hearts of rats. Oxygen consumption rate was measured polarographically at 37ºC using a Clark-type oxygen electrode with either glutamate/malate or succinate as energy substrates of Complex I or II, respectively. Levels of lipid hydroperoxides, reduced glutathione (GSH), superoxide dismutase (Mn-SOD) and cytochrome c oxidase activity were determined in mitochondrial preparations.

**Results and discussion.** Respiration studies on isolated heart mitochondria revealed that estrogen deficiency decreased the respiratory control index (RCI; state 3/state 4) for Complexes I and II by 26 % and 34%, respectively, and cytochrome c oxidase activity compared to intact control. HFD feeding induced a decrease of RCI for Complex I in OVX animals by44%, but did not significantly affect succinate oxidation (Complex II) in the state 3 and the state 4 of respiration. Administration of $E_2$ increased RCI for Complex I, normalised the ratio of state 3 to state 4 respiration at Complex II and cytochrome c oxidase activity. In addition, $E_2$ provided also 50% reduction in lipid hydroperoxides contents, enhanced Mn-SOD activity and normalised GSH level in heart mitochondria of ovariectomised rats with fructose-induced insulin resistance.

**Conclusion.** These data demonstrate 17β-estradiol replacement inhibited the development of mitochondrial dysfunction and oxidative stress in the heart of ovariectomised rats with fructose-induced insulin resistance.