Flavocoxid protects against cadmium-induced disruption of the blood-testis barrier and improves testicular damage and germ cell impairment in mice

M. Rinaldi[1], L. Minutoli[1], A. Micali[2], A. Pisani[2], D. Puzzolo[2], A. Bitto[1], G. Pizzino[1], N. Irrera[1], F. Galfo[1], G. Pallio[1], A.M. Mecchio[1],H. Marini[1], F. Squadrito[1], D. Altavilla[3]

[1]Dept. of Clinical and Experimental Medicine, University of Messina, Italy
[2]Dept. of Biomedical Sciences and Morphological and Functional Images, University of Messina, Italy
[3]Dept. of Paediatric, Gynaecological Microbiological and Biomedical Sciences, University of Messina, Italy

Cadmium (Cd) causes male infertility. There is the need to identify safe treatments counteracting this toxicity. Flavocoxid is a flavonoid that induces a inhibition of COX-1 and COX-2 and of 5-LOX. It has been show to be effective in the male genitourinary system. We investigated the effects of flavocoxid on Cd-induced testicular toxicity in mice.
Mice were divided into four groups: two control groups received 0.9% NaCl (vehicle; 1 ml /kg/day) or flavocoxid (20 mg/kg/day i.p.); two groups were challenged with cadmium chloride ($CdCl_2$; 2 mg/kg/day i.p.) and administered with vehicle or flavocoxid. The treatment lasted for one or two weeks. The testes were processed for biochemical and histological studies. $CdCl_2$ increased p-ERK 1/2, TNF-α, COX-2, 5-LOX, MDA, Bax, FSH, LH, TGF-β3, decreased Bcl-2, testosterone, inhibin-B, occludin, N-Cadherin, and induced structural damages in the testis. Many TUNEL-positive germ cells were present. Flavocoxid reduced p-ERK 1/2, TNF-α, COX-2, 5-LOX, MDA, Bax, FSH, LH, TGF-β3, augmented Bcl-2, testosterone, inhibin B, occludin, N-Cadherin, and improved the structural organization of the testis. Few TUNEL-positive germ cells were present.
Considering the extensive exposure to Cd, we suggest that flavocoxid may play a relevant positive role against environmental levels of Cd, otherwise deleterious to gametogenesis.