

Flavocoxid mitigates cadmium-induced toxicity: structural, immunohistochemical and molecular analysis in mice kidney

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Background: Cadmium (Cd), a diffused environmental pollutant, has adverse effects on urinary apparatus [1]. The role of flavocoxid, a flavonoid with antioxidant activity [2], on the morphological and biochemical changes *induced in vivo* by Cd in mice kidneys was evaluated.

Methods: C57 BL/6J mice received 0.9% NaCl alone, flavocoxid (20 mg/kg/day i.p.) alone, Cd chloride (CdCl2) (2 mg/kg i.p.) alone, or CdCl2 plus Flavocoxid (2 mg/kg i.p. plus 20 mg/kg/day i.p.) for 14 days. At the end of experiment, the mice were killed with an overdose of ketamine and xylazine and the kidneys were collected and processed for structural, immunohistochemical and biochemical analysis.

Results: Cd treatment alone significantly increased iNOS, TNF- α and MMP-9 expression, induced structural damages in the glomeruli and in the proximal tubule epithelium, and reduced claudin-11, occludin and N-cadherin immunoreactivity. Flavocoxid administration reduced iNOS, TNF- α and MMP-9 expression, ameliorated glomerular and tubular changes and enhanced claudin-11, occludin and N-cadherin immunoreactivity.

Conclusions: We demonstrated for the first time that flavocoxid has a protective role against Cd-induced damages in mice kidney. Therefore, flavocoxid may have a promising role against environmental Cd, in particular against its harmful effects on glomerular and tubular lesions.

References

- [1] Yang H, Shu Y. (2015) Cadmium transporters in the kidney and cadmium-induced nephrotoxicity. Int J Mol Sci 16:1484-1494.
- [2] Minutoli L, Micali A, Pisani A, et al. (2015) Flavocoxid protects against cadmium-induced disruption of the blood-testis barrier and improves testicular damage and germ cell impairment in mice. Toxicol Sci 148:311-329.

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Cadmium, flavocoxid, kidney, glomeruli, tubular epithelium, light microscopy, immunohistochemistry, Western blot analysis

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