but when given together MDA and GSH concentrations increased (0.20 ± 0.02; 7.88 ± 0.93 μmol L^{-1}, mean ± SD, $P < 0.05$) as compared to controls (0.16 ± 0.02; 14.68 ± 5.21 μmol L^{-1}). When given alone OTA did not affect parameters of hOGG1 comet assay either in kidney or in liver homogenates, while CTN increased tail intensity in kidney ($1.65 \pm 0.32\%$) as compared to controls ($0.72 \pm 1.02\%$). OTA and CTN given together significantly increased tail intensity in kidney ($5.33 \pm 1.55\%$, contr. $1.99 \pm 0.65\%$) and liver ($4.10 \pm 0.82\%$, contr. $1.04 \pm 0.11\%$) and tail length in kidney (14.27 ± 1.50 μm, contr. 12.64 ± 0.51 μm). Our results indicate that oxidative stress increases significantly when OTA and CTN are given together.

doi:10.1016/j.toxlet.2011.05.756

P2133
Renal proximal tubular reabsorption is reduced in adult rats treated with CsA: Roles of superoxide and Na+/H+ exchanger 3

S. Damiano [1], R. Ciarcia [2], R. Scanni [1], G.E. Granato [2,*], F. Fiorito [3], G. Capasso [1], S. Florio [4]

[1] *Internal Medicine - Division of Nephrology, Second University of Naples, Naples, Italy*, [2] *Structures, Function and Biological Technologies, University of Naples, Naples, Italy*, [3] *Pathology and Animal Health, University of Naples, Naples, Italy*, [4] *Structures, Function and Biological Technologies, University of Naples "Federico II", Naples, Italy*

Cyclosporine A (CsA) is used for preventing graft rejections and autoimmune disease. Unfortunately, its use is hampered by nephrotoxic effects including hypertension. It was shown that CsA-nephrotoxicity is due to an increase in ROS. We decided to test the effects of the inhibitor of NADPH oxidase, Apocynin (Apo) in rats treated with CsA by in vivo and in vitro study. In particular we studied the alteration in the proximal tubule (PT), because changes in PT reabsorption may contribute to the development of hypertension. *Methods*: In situ microperfusion. Rats were treated with Csa, Csa + Apo, Apo and PBS for 21 days and then they were anaesthetised and prepared for micropuncture of the left kidney. The PT site was identified by injections of a dye-stained artificial tubular fluid and it was perfused at 20 ± 3 nl/min. Tubule fluid collections were made at a downstream site. The absoluted fluid reabsorption (Jv) was calculated by the difference in the perfusion rate and the collection rate factored by the length of the nephron. Western blot analysis. We used the primary antibody for Na+/H+ exchanger 3 (NHE3) to evaluate the molecular mechanism of Jv alteration. We have found that fluid reabsorption and NHE3 expression in the PT of CsA rats is impaired compared with control. Apo restored these levels. These data suggest that Jv is regulated by O2-reduction of NHE3. It is possible that O2-regulated PT absorption by interaction with nitric oxide that induce a reduction of bioavailable of NO that should inhibit Jv in the proximal tubule.

doi:10.1016/j.toxlet.2011.05.757

P2134
Hydrocortisone modulates the production of nitric oxide and the activity of the antioxidant enzymes in the kidney of rats treated with cyclosporine

R. Ciarcia [1], G.E. Granato [1,*], S. Damiano [2], F. Fiorito [3], R. Russo [4], S. Montagnaro [4], L. Manco [1], S. Florio [5]

[1] *Structures, Function and Biological Technologies, University of Naples, Naples, Italy*, [2] *Internal Medicine - Division of Nephrology, Second University of Naples, Naples, Italy*, [3] *Pathology and Animal Health, University of Naples "Federico II", Naples, Italy*, [4] *Pathology and Animal Health, University of Naples, Naples, Italy*, [5] *Structures, Function and Biological Technologies, University of Naples "Federico II", Naples, Italy*

Cyclosporine (CsA) can be considered the prototype of immunosuppressant that has revolutionized the management of allotransplantation. Nephrotoxicity and hypertension are the major adverse effects that often limit CsA treatment following solid organ transplantation and autoimmune diseases. Experimental data suggest a role for reactive oxygen metabolites as one of the postulated mechanisms in the pathogenesis of CsA nephrotoxicity. This study was designed to examine the possible beneficial effects of hydrocortisone (HY) in preventing the acute renal failure and related oxidative stress caused by chronic administration of CsA in rats. HY was injected intraperitoneally (5 mg/kg/die/2 ml) concurrently with CsA (25 mg/kg/day subcutaneously for 28 days). The malondialdehyde (MDA) content, a measure of lipid peroxidation, was assayed in kidney, by means of the thiobarbituric acid test, reduced glutathione content, superoxide dismutase and catalase. Nitrite levels were estimated in tissue homogenates. The treatment with CsA for 28 days produced elevated levels of MDA from 149.7 ± 37.5 to 283.4 ± 53.9 pmol/mg of proteins. HY decreased MDA concentration CsA-induced from 283.4 ± 53.9 to 179.3 ± 19.2 pmol/mg of proteins and significantly induced a depletion of renal endogenous antioxidant. The treatment with CsA alone decreased the nitric oxide (NO) production from 13.9 ± 3.7 to 6.7 ± 0.9 pmol/mg of proteins while HY synergically decreased NO CsA-induced from 6.7 ± 0.9 to 4.3 ± 0.5 pmol/mg of proteins. Our results suggest that CsA nephrotoxicity was attenuated by treatment with HY and suggests the role of oxidative stress in the pathogenesis of CsA-induced nephrotoxicity.

doi:10.1016/j.toxlet.2011.05.758

P2135
Comparative study of antioxidative stress of estradiol, α-lipoic acid and L-carnitine against carbon tetrachloride-induced hepatotoxcity in rats

M.A. Hamzawy [1,*], E.S.M. El-Denshary [2], M.A. Abdel-Wahhab [3], N.S. Hassan [4], A.K. Bahgat [2]

[1] *Pharmacology & Toxicology, College Pharmacy, Misr University for Science & Technology, 6th October, Egypt*, [2] *Pharmacology & Toxicology, Faculty of Pharmacy, Cairo University, Cairo, Egypt*, [3] *Food Toxicology & Contaminants, National Research Center, Cairo, Egypt*, [4] *Pathology, National Research Center, Cairo, Egypt*

Propose: The aim of the current study was to compare the hepatoprotective potential of estradiol, α-lipoic acid and L-carnitine against carbon tetrachloride CCl_4-induced liver damage. *Methods*: Eight groups of male Sprague–Dawley rats were treated for 4 weeks as follows: the control group, the group treated with CCl_4 and the