POSSIBLE MECHANISM RESPONSIBLE FOR ALLOPURINOL-NEPHROTOXICITY:
LIPID PEROXIDATION AND SYSTEMS OF PRODUCING- AND SCAVENGING
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In order to elucidate toxic and protective mechanisms
responsible for allopurinol-induced nephrotoxicity in rats, we
investigated changes in plasma creatinine concentration, in
renal lipid peroxidation, and in renal activities of xanthine
oxidase, superoxide dismutase and catalase, as enzymatic
factors in producing and scavenging oxygen radicals. The rats
received subcutaneous injections of allopurinol in a dose of
100 mg/kg body weight, once a day for 3 days. In comparison
to the control rats, the following changes were observed in
the allopurinol-administered rats: increases in plasma
creatinine concentration, in renal contents of malonaldehyde,
hypoxanthine and xanthine, and in renal activity of xanthine
oxidase, and decreases in renal activities of superoxide
dismutase and catalase. Peaks in these changes were observed
coincidently in the third day after the starting of the
administration. Afterwards, these all returned to the control
levels. These results strongly suggested that the allopurinol
nephrotoxicity was attributed to the increase of lipid
peroxidation which had been caused both by an increase in the
ability of producing the oxygen radicals and by a decrease in
the ability of scavenging the radicals.

STUDIES ON THE MECHANISM OF NEPHROTOXICITY OF AMINOGLYCOside ANTIBIOTICS III.
EFFECTS ON CULTURED RENAL EPITHELIAL CELLS: Ken-ichi KIYOMIYA, Naoko MATSUMIHATA
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We have previously reported that administrations of gentamicin (GM), amikacin
(AMK) or streptomycin (SM) to rats for 8 days increase urinary excretion of
calium, glucose, protein, brush border membrane enzymes, cytoplasmic enzymes
and lysosomal enzyme and induce histopathological lesions in proximal
epithelial cells. This study was performed to investigate on the nephrotoxicity of
aminoglycoside antibiotics in cultured LLC-PK1 cells, pig kidney proximal
cell line in comparison with rats.

An addition of GM, AMK or SM (1 mM each) into culture medium caused release of
enzymes from brush border membrane (alkaline phosphatase, γ-glutamyl
transpeptidase), cytoplasm (lactate dehydrogenase) and lysosome (N-acetyl-β-D-
glucosaminidase) in LLC-PK1 cells during cultivation. The treated cells
contained lower activity of brush border membrane enzymes and lysosomal enzyme
and higher activity of cytoplasmic enzymes than untreated cells. Furthermore, 3H-
thymidine incorporation into the acid-insoluble fraction increased in
aminoglycoside antibiotic-treated cells. A treatment with aminoglycoside
antibiotics also resulted in an increase of total phospholipid content in the
cells and an inhibition of 45Ca uptake by the cells.

These results lead to the conclusion that intensity and character of
nephrotoxicity of aminoglycoside antibiotics in cultured LLC-PK1 cells are
similar to those in rats. The intensity order of nephrotoxicity in these
antibiotics was GM > AMK > SM.