ing media. Morphologically noted are accumulation of lipid droplets and polyribosomal dispersion, which may be association with inhibition of cellular synthetic activity.

These results suggest the toxicity is a direct effect of cyclosporine and that toxic mechanism may be due to inhibition of cellular synthetic activity. And this experiment also showed that primary cultures of human renal proximal tubular cells can be a good in vitro model for investigating CsA nephrotoxicity.

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Kinetics of Cyclosporine Uptake on Cultured Human Porximal Tubular Cells

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Cyclosporine A (CsA), a lipophilic cyclic undecapeptide, is not accumulated evenly in all tissues and has a high affinity to several tissues such as lymphoid organs, liver, and kidneys. From this point of view, it is reasonable to assume that the amount of CsA uptake would be correlated with the extent of cell injury. On the other hand, verapamil, a Ca^{2+} channel blocker, has been shown to ameliorate CsA nephrotoxicity. Since proximal tubule is the major site of drug transport and CsA toxicity, the author has studied the nature of CsA uptake and its interaction with verapamil in isolated human renal proximal tubular cells.

The CsA uptake pattern showed rapid increse over the first 5 min, and then achieved almost steady-state after 10 min all conentrations (0.5~10 uM). And the Ca^{2+} free state in media enhanced CsA uptake significantly, but there was no difference between the uptake of 2.5 mM and normal (1.8 mM) Ca^{2+} levels in the media. Kineic analysis yielded that the Km and Vmax values of cyclosporine were 5.6 uM and 86.2 p mol/ug cell protein/min, respectively. And verspamil (0.5 and 1 uM) reduced CsA uptake significantly (82 and 42% of control, respectively). But A_2 3187 had no effect on CsA uptake.

These results suggest that the calcium channels and CsA transporting sites on cell membrane are closely associated, and that Ca and CsA might be uptaken competitively by proximal tubular cells.

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Effect of Cadmium Intoxication on Renal Phosphate Transport System in Rats

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Effect of cadmium intoxication on the renal cortical phosphate transport system was studied in adult male Sprague-Dawley rats. Subcutaneous injections of cdcl at a dose of 2 mg cd/kg body weight per day for 2 weeks induced marked polyuria, glycosuria, proteinuria and phosphaturia, which are the characteristics of chronic cadmium intoxication. In the renal cortical brush-border membrane vesicles prepared from cadmium-intoxicated rats, the Na^+-dependent phosphate uptake was markedly attenuated, whereas the Na^+-independent uptake was not apparently altered. These results indicates that cadmium intoxication impairs the Na^+-phosphate cotransport system in the brush-border membrane of renal proximal tubular cells, which leads to phosphaturia in intact animals.