Table 1: Effect of CMN on cyclosporine-induced nephrotoxicity

Variables	*Control*	*CsA (20)*	*CMN(15)*	*CsA (20)+ CMN(5)*	*CsA (20)+ CMN(10)*	*CsA (20)+ CMN(15)*
Serum creatinine (mg/dl)	0.95 ± 0.01	3.12 ± 0.17[a]	0.87 ± 0.01[b]	2.00 ± 0.11[a,b]	1.5 ± 0.06[a,b]	1.00 ± 0.01[a,b]
Creatinine clearance (ml/min)	0.76 ± 0.06	0.078 ± 0.05[a]	0.87 ± 0.05[b]	0.44 ± 0.03[a,b]	0.65 ± 0.04[a,b]	0.80 ± 0.05[b]
BUN (mg/dl)	24.55 ± 0.77	87.44 ± 4.37[a]	26.87 ± 0.64[b]	73.65 ± 1.32[a,b]	53.21 ± 0.9[a,b]	35.89 ± 0.64 [a,b]
Urea clearance (ml/min)	0.58 ± 0.04	0.19 ± 0.05[a]	0.61 ± 0.03[b]	0.49 ± 0.02[a,b]	0.53 ± 0.03[a,b]	0.59 ± 0.03[b]

Values are expressed mean ± mean. a = Statistical significant at P < 0.05 as compared to control, b = Statistical significant at P < 0.05 as compared to Cyclosporine (CsA)

Table 2: Effect of CMN on cyclosporine-induced Nitrite levels

Variables	*Control*	*CsA (20)*	*CMN(15)*	*CsA (20)+ CMN(5)*	*CsA (20)+ CMN(10)*	*CsA (20)+ CMN(15)*
Serum Nitrite(μmol/ml)	62 ± 3.72	91.9 ± 50.6[a]	60 ± 3.15[b]	77 ± 4.55[a,b]	69 ± 8.75[b]	61 ± 3.05[b]
Tissue nitrite(μmol/mg)	103.518 ± 2.73	190.656 ± 7.97[a]	101.814 ± 2.27[b]	174.704 ± 4.01[a,b]	144.79 ± 3.01[a,b]	116.912 ± 2.27[a,b]

Values are expressed mean ± mean. a = Statistical significant at P < 0.05 as compared to control, b = Statistical significant at P < 0.05 as compared to Cyclosporine (CsA)

Cumulative data suggest a role for reactive oxygen metabolites as one of the postulated mechanisms in the pathogenesis of CsA nephrotoxicity. CsA results in enhanced generation of hydrogen peroxide in cultured hepatocytes [5] and mesangial cells [6,7]. In vitro and in vivo studies indicate that CsA enhances lipid peroxidation, reduces renal microsomal NADPH cytochrome P450, and renal reduced/oxidized glutathione ratio (GSH/GSSG) in kidney cortex as well as renal microsomes and mitochondria [8-11]. Antioxidants such as α-tocopherol, ascorbate, silibinin, lazaroid, propionyl carnitine and superoxide dismutase/catalase, have been shown to ameliorate cyclosporine-induced renal toxicity [5,12].

Current traditional Indian medicine claims the use of *Curcuma longa* L. *(Zingiberaceae)* powder against biliary disorders, anorexia, coryza, cough, diabetic wounds, hepatic disorder, rheumatism and sinusitis [13]. Curcumin (CMN) is a major component in curcuma/turmeric, being responsible for its biological actions. More and more studies now show that CMN exhibit anti-inflammatory[14,15], anti-human immunodeficiency virus [16,17], anti-bacterial [18] and nematocidal activities [19]. Various *in-vitro* and *in-vivo* studies increasingly establish the antioxidant properties of CMN [20-22]. It is well documented that CMN scavenges superoxide anions [23], peroxynitrite radicals [24,25], and quenches singlet oxygen [26]. CMN has also been shown to inhibit hydrogen-peroxide-induced cell damage [20].

Thus the present study was designed to examine the possible beneficial effect of CMN in preventing the acute renal failure and related oxidative stress caused by chronic administration of CsA in rats.

Results

Effect of CMN on renal function

CsA treatment for 21 days significantly increased the serum creatinine and blood urea nitrogen (BUN) as compared with the control group. Chronic CMN treatment significantly and dose-dependently prevented this rise in BUN and serum creatinine (Table-1). Moreover, the creatinine and urea clearance, which was markedly reduced by CsA-administration, was significantly and dose-dependently improved by CMN treatment (Table-1). However, CMN (15 mg/kg) *per se* had no effect on serum creatinine, BUN, creatinine and urea clearance.

Effect of CMN on CsA-induced nitrosative stress

Serum and tissue nitrite levels were significantly elevated by CsA-administration. Curcumin treatment significantly and dose dependently improved this increase in nitrite levels both in serum and tissue (Table-2). However, CMN (15 mg/kg) *per se* had no effect on serum nitrite levels.

Effect of CMN on CsA-induced lipid peroxidation

Renal TBARS levels were markedly increased by CsA administration as compared to control group. Treatment with curcumin produced a significant and dose-dependent reduction in TBARS in CsA-treated rats, however curcumin per se did not alter TBARS (Fig. 1).