Background. The present study was conducted to investigate whether caffeic acid phenethyl ester (CAPE), an active component of propolis extract, has a protective effect on amphotericin B induced nephrotoxicity in rat models. Methods. Male Wistar-Albino rats were randomly divided into four groups: (I) control group (n = 10); (II) CAPE group (n = 9) received 10 µmol/kg CAPE intraperitoneally (i.p.); (III) amphotericin B group (n = 7) received one dose of 50 mg/kg amphotericin B; and (IV) amphotericin B plus CAPE group (n = 7) received 10 µmol/kg CAPE i.p. and one dose of 50 mg/kg amphotericin B. CAPE started one day before the administration of amphotericin B and continued for 7 days. The left kidney was evaluated histopathologically for nephrotoxicity. Levels of malondialdehyde (MDA), nitric oxide (NO), enzyme activities including catalase (CAT) and superoxide dismutase (SOD) were measured in the right kidney. Results. Histopathological damage was prominent in the amphotericin B group compared to controls, and the severity of damage was lowered by CAPE administration. The activity of SOD, MDA, and NO levels increased and catalase activity decreased in the amphotericin B group compared to the control group (P=0.0001, P=0.003, P=0.0001, P=0.0001 respectively). Amphotericin B plus CAPE treatment caused a significant decrease in MDA, NO levels, and SOD activity (P=0.04, P=0.002, P=0.0001 respectively) and caused an increase in CAT activity compared with amphotericin B treatment alone (P=0.005). Conclusion. CAPE treatment seems to be an effective adjuvant agent for the prevention of amphotericin B nephrotoxicity in rat models.