The present study was to evaluate the protective effect of melatonin against aluminum induced neurotoxicity in cerebral cortex of albino mice. Male albino mice were divided into four groups. Group I treated as control, Group II intraperitoneally injected with aluminum acetate (Al) (3.5 mg/kg body weight (b.w.)), Group III mice were administered with melatonin (Mel) (7mg/kg b.w.i.p.) and Group IV animals were given aluminum plus melatonin for 6 weeks. At the end of the treatment cerebral cortex was removed and processed to examine the oxidative stress markers: superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GR), reduced glutathione (GSH), glutathione peroxidase (GPx) and glutathione-s-transferase (GST) and thiobarbituric acid-reactive substances (TBA-RS). Histopathology was examined using light and electron microscopic studies. Al exposure promotes oxidative stress significantly, estimated by increase in TBA-RS and decrease in the activities of SOD, CAT, GR, GSH, GPx and GST. In contrast, Mel significantly decreased the aluminum-induced oxidative damage in the cortex of albino mice. Protective effects of Mel were also observed at microscopic level. Light and electron microscopic studies revealed the remarkable nuclear changes within neurons, deprival of neuronal integrity and ultra structural changes were associated with Al administration, which however were decreased appreciably following Mel supplementation. The results of the present investigation emphasize the potential use of melatonin has the ability to prevent of free radical based neurological disorders in which oxidative stress is involved by virtue of its antioxidant activity.