Bleomycin is an anti-neoplastic antibiotic drug that produces dose and time dependant pulmonary fibrosis. Several studies reported the important role of angiotensin II type 1 (AT1) receptor blockers in suppressing fibrosis in different organs, therefore, the current study aimed to examine the protective role of irbesartan against bleomycin-induced pulmonary fibrosis in rats. The effect of irbesartan on the serum and tissue levels of growth factors and plasminogen activator inhibitor-1 (PAI-1) has been studied. Oral administration of irbesartan (10, 20 or 40 mg/kg/day) for 21 days, starting from the first day of bleomycin injection (10 mg/kg/day/10 days, i.p.) attenuated the severity of bleomycin-induced pulmonary fibrosis, decreased the expression of α-smooth muscle actin and enhanced the histopathological features of the lung. Furthermore, irbesartan decreased serum transforming growth factor-β1 and increased serum as well as tissue level of vascular endothelial growth factor compared to bleomycin group (P < 0.05). Importantly, treatment with all the dose levels of irbesartan did not affect immunohistochemical staining for AT1 receptors in lung tissues. Moreover, treatment with irbesartan (20 mg/kg/day) decreased mRNA expression of PAI-1 in lung tissues compared to bleomycin-treated group. The present study concluded for the first time that the ameliorating effect of irbesartan on bleomycin-induced pulmonary fibrosis in rats involves modulation of growth factors and reduction of the mRNA expression of PAI-1.

**Keywords:** Bleomycin, Growth Factors, Irbesartan, Plasminogen activator inhibitor-1, Rat.