The relationship between Erectile Dysfunction (ED) and Chronic Renal Failure (CRF) has been reported in several studies. The present study aimed to investigate whether the chronic use of sildenafil could enhance the erectile capacity in CRF-induced rats. Additionally, we assessed the effect of that treatment on some molecules, which have been suggested to play crucial roles in erectile physiology and CRF related ED as well. Three groups of animals were utilized: (1) age-matched control rats, (2) CRF induced rats, (3) CRF-induced rats treated with chronic administration of sildenafil [5mg/kg p.o for 6 weeks (treatment started after 6 weeks of CRF induction)]. At three months, all animals underwent cavernosal nerve stimulation (CNS) to assess erectile function. Penile tissue Advanced Glycation End Products (AGE’s/5-HMF), Malondialdehyde (MDA), cGMP (ELISA), iNOS and nNOS (Western Blot) analyses were performed in all groups of rats. CRF-induced rats had a significant decrease in erectile function as determined by the peak intracavernosal pressure (ICP) and total ICP (area under the curve; AUC) after CNS when compared to control rats (p<0.05). The increase in both ICP and AUC of CRF-induced rats treated with sildenafil (Group-3) was greater then CRF-induced rats (Group-2). Additionally, sildenafil treatment decreased AGE, MDA and iNOS levels, while it preserved nNOS and cGMP contents in CRF-induced penile tissue. Decreased AGE, MDA, iNOS and increased nNOS, cGMP levels at the sildenafil treated group increased both ICP and Total ICP to CNS, which lead to improved erectile function in CRF-induced rats. The results of the present study revealed the therapeutic effect of chronic sildenafil administration on erectile function in CRF-induced rats.