Objectives: The present study aimed to investigate the effects of a novel lipoic acid derivative drug sodium zinc dihydrolipoylhistidinate (DHLHZn) on atrial fibrosis and fibrillation (AF) which is associated with chronic kidney disease (CKD). Methods: Male Sprague-Dawley rats were subjected to 5/6 nephrectomy (5/6Nx) or sham operation (Control: CNT). DHLHZn (5 mg/kg/day) were subcutaneously and continuously infused by osmotic mini-pump. Four weeks later, hearts were isolated for assessment of left atrial (LA) interstitial fibrosis and AF vulnerability. Results: 1) 5/6Nx induced renal dysfunction with elevation of systolic and diastolic blood pressure (p<0.05). 2) When compared to CNT group, extensive and heterogeneous LA interstitial fibrosis was observed in 5/6Nx group (p<0.01), which was attenuated by DHLHZn (p<0.05). 3) In isolated perfused heart experiments, 5/6Nx caused slowing of interatrial conduction without affecting atrial refractoriness. In 5/6Nx hearts, right atrial extrastimuli invariably induced AF (100%), which were suppressed by DHLHZn (33%, p<0.05). Conclusions: We have succeeded to create an appropriate rat AF model associated with CKD. Because DHLHZn, a potent antioxidant agent, was effective, oxidative stress may be involved in the pathogenesis of LA fibrosis and AF in our CKD model. Keywords: atrial fibrillation, chronic kidney disease, lipoic acid derivative drug