SUMMARY AND CONCLUSIONS
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The present study was undertaken to investigate the role of nitric oxide in experimental renal failure. The protective effect of nitric oxide donors in ischemia/reperfusion renal damage, cyclosporine-induced nephrotoxicity, glycerol-induced myoglobinuric acute renal failure, subtotal nephrectomized-induced progressive renal damage, chronic nitric oxide synthase (NOS) inhibition-induced hypertension and renal damage and renal ischemic preconditioning was studied.

On the basis of the results, the salient findings of the study can be summarized as:

1. Nitric oxide has a crucial role in the pathogenesis of ischemic, nephrotoxic & myoglobinuric renal failure as well as in chronic renal failure. This was evident from the decrease in tissue and urinary total nitric oxide levels coupled with deterioration of renal function, enhanced oxidative stress and disrupted renal morphology in these experimental paradigms. Pharmacological agents which increase the endogenous nitric oxide levels such as L-arginine, molsidomine or nebivolol and agents which upregulate the nitric oxide synthase activity such as resveratrol and pravastatin can be of potential value in the treatment of renal failure.

2. The decrease/inhibition of the activity of nitric oxide synthase, particularly that of eNOS is responsible for the development of renal failure, as L-NIO, a specific eNOS inhibitor, ameliorated the protective effect observed with these pharmacological agents.

3. Chronic inhibition of nitric oxide synthase leads to development of hypertension and subsequently to renal damage. Chronic NO inhibition disrupts the delicate balance between the steady state levels of NO and \( \text{O}_2^- \) in favor of vasoconstrictors. NO donors and eNOS upregulators shift this balance towards NO and arrest the hypertensive renal damage.

4. Three repetitive cycles of 2 minutes of renal ischemia separated by 5 minutes of reperfusion period precondition the rat kidney and ameliorate the structural as well as functional damage. The findings strongly support the view that eNOS-mediated NO production plays a pivotal role in the protective effect of IPC as the
renal-protecting effects of ischemic preconditioning were blocked by pretreatment with the specific eNOS inhibitor (L-NIO), but not with the relatively selective iNOS inhibitor, aminoguanidine.

The findings of our study strongly emphasize that in renal failure, there is marked decrease in endogenous nitric oxide levels. The pharmacological agents which can increase the nitric oxide directly or the agents which can upregulate the enzyme NOS, particularly the eNOS may be beneficial in the settings of acute as well as chronic renal diseases. Further, the phenomenon of ischemic preconditioning, renders the rat kidney tolerant to the subsequent ischemia/reperfusion-induced (I/R) injury, possibly via the involvement of eNOS.