



## Nephrotoxic effects of bacterial ribonucleases in the isolated perfused rat kidney

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### Abstract

Alterations of the renal function in the isolated perfused rat kidney system after application of two bacterial RNases, *Bacillus intermedius* RNase (binase) and ribonuclease produced by *Bacillus amyloliquefaciens* (barnase), were investigated with two different treatment regimens in comparison with catalytically inactive derivatives of the enzymes, photooxidated at the active site His<sup>101</sup> binase and inactive mutant His<sup>102</sup>Gln barnase. For the in vitro approach the test enzymes were dissolved in the perfusion media and applied to the kidney after removal from the animal. Alternatively, the test ribonucleases were administered to rats in vivo and the renal effects were assessed in the isolated perfused rat kidney 1 and 6 h after treatment. In the in vitro regimen both active enzymes induced time- and concentration-dependent nephrotoxicity reflected in enhancement of urinary protein excretion, decline of glucose reabsorption, increase of  $\gamma$ -glutamyltranspeptidase and alkaline phosphatase activities in urine. In vivo administration of active binase induced functional impairment of the isolated perfused organ in a similar way. None of the inactive RNases in both regimens and at all concentrations tested altered any renal parameter. The results suggest that RNA degradation may be involved in the nephrotoxic effects of bacillar RNases. © 1997 Elsevier Science Ireland Ltd.

**Keywords:** *Bacillus intermedius* RNase (binase); *Bacillus amyloliquefaciens* ribonuclease (barnase); Photoinactivated binase; His<sup>102</sup>Gln barnase; Isolated perfused rat kidney; Nephrotoxicity

### 1. Introduction

**Abbreviations:** ALP, alkaline phosphatase; barnase, *Bacillus amyloliquefaciens* ribonuclease; binase, *Bacillus intermedius* RNase;  $\gamma$ -GT,  $\gamma$ -glutamyltranspeptidase.

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Extracellular ribonuclease from *Bacillus intermedius* (binase) and ribonuclease produced by *Bacillus amyloliquefaciens* (barnase) have high homology in primary structure and share similar