



## OXIDATION OF URATE BY A THERAPEUTIC NITRIC OXIDE/AIR MIXTURE

Mark Hicks\*<sup>1</sup>, Peter Rogers<sup>2</sup>, Ly Nguyen<sup>1</sup> and Richard Day<sup>1</sup>*<sup>1</sup>Department of Clinical Pharmacology and Toxicology and <sup>2</sup>Department of Respiratory Medicine, St Vincent's Hospital, Victoria St, Darlinghurst, NSW 2010, AUSTRALIA.*

Little is known about the potential toxicological consequences of therapeutic exposure of lung tissue to inhaled nitric oxide (NO). This route of administration is currently being successfully employed for the treatment of pulmonary hypertension and other lung pathologies including acute reperfusion injury in lung transplant patients. The toxicity of NO lies in its ability to act as an oxidant either in its own right or in concert with oxygen or with the superoxide free radical. One important interaction may be the reaction of these products with protective antioxidants in the lung epithelial lining fluid. One such antioxidant found in significant concentrations in both upper and lower airways is uric acid. In the present study, urate solutions (30 $\mu$ M) were exposed to a therapeutic concentration of NO gas, (35 ppm in air), for up to 90 minutes. Oxidative changes were followed spectrophotometrically and by HPLC. Significant loss of uric acid was observed with a concomitant formation of nitrite and allantoin, the stable oxidation product of NO and the major oxidation product of uric acid, respectively. No oxidation of urate was observed in the presence of air alone or when urate was incubated with nitrite. Uric acid oxidation could also be prevented by passing the NO / air stream through 10% KOH before the uric acid solution. This strategy removed trace amounts of higher oxides of nitrogen, (especially NO<sub>2</sub>), from the NO / air stream. Thus, therapeutic inhalation of NO may deplete soluble antioxidants such as uric acid, especially during long-term chronic exposure unless care is taken to minimise formation of higher oxides of nitrogen.