# NITRIC-OXIDE SCAVENGING PROPERTIES OF NOVEL ORGANIC COMPOUNDS CONTAINING COBALT(II) AND RUTHENIUM(III)

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**Background**: Excessive NO production as usually occurs as a consequence of nitric oxide synthase type II (NOS II) induction represents a key pathophysiologic event in chronic inflammatory diseases, neurodegenerative diseases and septic shock. Thus, new molecules that could blunt harmful endogenous NO levels may represent a good chance to reduce tissue damage during these critical hills. Since the poor selectivity of NOS II inhibitors results in the blockade of constitutive NOS, endothelial dysfunction and hypertension, an alternative approach to block the toxicity of high NO production is the use of NO scavengers, whose affinity to NO could be modulated to maintain NO concentration in the biological fluids below the toxicity threshold without interfere with other beneficial NO effects. Therefore, the aim of this study was to evaluated the possible scavenging role of several organic complexes containing metallic ions (iron, cobalt, ruthenium, manganese) that can rapidly form stable nitrosylic adducts. **Methods**: Anionic polyaminic scaffolds containing cobalt(II), ruthenium(III), iron(III) and manganese(II) were prepared in the Department of Chemistry of the University of Florence and preliminarily tested for their efficiency to bind gaseous NO; the stability of the NO adducts was also evaluated in time-course by UV-vis spectrophotometry. Scavenging properties of selected molecules were then evaluated on macrophagic line RAW 264.7 after induction of NOS II by 24h pretreatment with LPS/cytokine cocktail. Nitric oxide quantity (in control condition and in the presence of different concentration of scavanging molecules) was evaluated as nitrite accumulation for 18h using the Griess reagent. **Results and Discussion**: Treatment of RAW 264.7 with LPS/cytokine cocktail markedly increased nitrite production from 0.9±0.24 nmol/ml/18h to 29.1±3.08 nmol/ml/18h; this increasing rate of production was strongly reduced (90%) by the NOS II inhibitor 1μM 1400W. Co(II) and Ru(III) complexes dose-dependently (1-200μM) reduced nitrite accumulation, whereas the Mn(II) and Fe(III) complexes were practically ineffective. At the high dose tested Ru(III) and Co(II) complex showed a 70% inhibition of nitrite accumulation when the scaffold was EGTA-based, but only a 30% with EDTA-based scaffold. These data demonstrate that: 1) the effectiveness of metal-based complexes is dependent on the metal centre, but are also modulated by the scaffold; 2) these molecules are useful to NO scavenger and therefore could be proposed in those pathologies characterised by an elevated production of NO.