

NITROXYL (HNO/NO-) – AN ENIGMATIC MOLECULE WITH UNIQUE PROPERTIES AND PHARMACOLOGICAL POTENTIAL

Summary

Nitrogen oxides are involved in many physiological processes and have the potential to be useful pharmacological agents. The discovery that nitric oxide (NO) is endothelial derived relaxing factor (EDRF) has led to an increase of research in this field. For many years, nitroxyl (HNO/NO⁻) which is one-electron reduction product of NO, has been overlooked, probably because no mechanism of endogenous *in vivo* HNO production has been clearly established – mainly due to a lack of a direct detection method of the compound. It is inherently unstable molecule so the studies on its biological properties must be done with the use of donor compounds. The most common donor currently used is Angeli's salt (Na₂N₂O₃), which releases HNO at physiological pH. It was shown that nitroxyl can react preferentially with ferric heme proteins and also with thiols and thus could influence the activ-

ity of many important enzymes with -SH groups in the active site. Similar to nitric oxide, nitroxyl has been shown to cause vasodilation and moreover, it has positive inotropic (force of muscle contraction) as well as lusitropic (relaxation of cardiac muscle) properties which both contribute to increased cardiac output. In addition to these effects HNO has been shown promising anticancer compound. It influences glycolysis process (nitroxyl inhibits activity of glyceraldehyde-3-phosphate dehydrogenase, GAPDH) which is a major energy source for cancer cells. Furthermore, HNO inhibits angiogenesis and induces cancer cell apoptosis. Because of unique properties of nitroxyl there has been a significant increase in interest in this molecule in the past few years. Herein, some of the chemical and biological activities and the pharmacological potential of HNO are described.