Nitrite reductase (NiR) is a type 2 copper-containing enzyme that reduces nitrite to nitric oxide as part of the global nitrogen cycle. Type 2 copper sites are found in a variety of versatile oxidoreductases that mediate reactions involving oxygen or nitrogen oxides and are found throughout all branches of life. Crystal structures of (NiR) to beyond 1.4 Å resolution with bound nitrite and nitric oxide have given insight into the catalytic mechanism which differs from that of heme cd1 NiR. Mutagenesis studies of copper NiRs show that an aspartate – histidine pair in the active site is found to control binding of copper ligands and largely define the chemical reactivity of NiR. Unexpectedly, nitrite and nitric oxide are bound in an almost face-on and side-on coordination to the copper. In contrast, the inhibitor azide binds end-on to the type 2 copper. Also, acetate and nitrate coordinate through both oxygens (bidentate), whereas nitrite is coordinated by a single oxygen that forms an H-bond to the active site aspartate, an interaction that is likely to be essential for efficient catalysis.

Interestingly, NiR is able to reduce oxygen to hydrogen peroxide in vitro, eventually leading to enzyme inactivation. The NiR type 2 copper site shares a similar coordination sphere to those of superoxide dismutase and amine oxidases suggesting the possibility of common mechanistic features with respect to reactivity of these sites with oxygen and nitrogen oxides.

**Keywords:** structures of metalloproteins, copper complexes, nitric oxide