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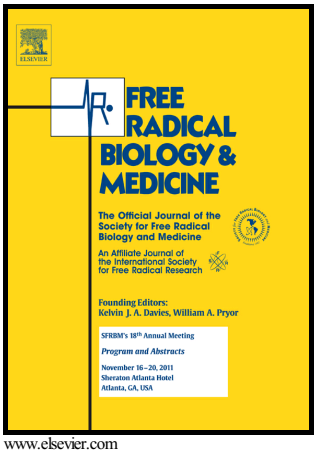

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Selenols are Resistant to Irreversible Modification by HNO

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Abstract

The discovery of nitric oxide (NO) as an endogenously generated signaling species in mammalian cells has spawned a vast interest in the study of the chemical biology of nitrogen oxides. Of these, nitroxyl (azanone, HNO) has gained much attention for its potential role as a therapeutic for cardiovascular disease. Known targets of HNO include hemes/heme proteins and thiols/thiol-containing proteins. Recently, due to their roles in redox signaling and cellular defense, selenols and selenoproteins have also been speculated to be additional potential targets of HNO. Indeed, as determined in the current work, selenols are targeted by HNO. Such reactions appear to result only in formation of diselenide products, which can be easily reverted back to the free selenol. This characteristic is distinct from the reaction of HNO with thiols/thiolproteins. These findings suggest that, unlike thiolproteins, selenoproteins are resistant to irreversible oxidative modification, indicating that Nature may have chosen to use selenium, instead of sulfur, in certain biological systems for this reason.

Abbreviations: Angeli's salt (AS), 2-bromopiloty's acid (2-BrPA), selenol (RSeH), selenocysteine (Sec), selenocystine (Sec_2), *N*-hydroxyselenenamide (RSeNHOH), seleneninamide ($RSe(O)NH_2$), 5,5'-Dithiobis(2-nitrobenzoic acid) (DTNB), cysteine (Cys_2), glutathione peroxidase (GPx), *o*-nitrophenylselenol (*o*-NPS), *bis*(*o*-nitrophenyl) diselenide (*o*-NPdS), benzeneselenol (PhSeH), diphenyl diselenide (PhSeSePh), selenocysteine methyl ester (SecOMe), selenocystine dimethyl ester ($SecOMe_2$)

Keywords: selenium, selenol, selenoenzymes, diselenide, seleninamide, *N*-hydroxyselenenamide, nitroxyl, thiol, disulfide, sulfinamide, *N*-hydroxysulfenamide, cysteine, selenocysteine, benzeneselenol