THE REACTIVITY OF HYPOTAURINE AND CYSTEINE SULFINIC ACID WITH PEROXYNITRITE*

Mario Fontana, Silvestro Duprè, and Laura Pecci**

1. INTRODUCTION

The oxidation of the sulfinic group of both hypotaurine and cysteine sulfinic acid with production of the respective sulfonate, taurine and cysteic acid is a crucial point for the generation of taurine in mammalian tissues (Wright *et al*., 1986; Huxtable, 1992). It has been proposed that the high levels of taurine found in tissues or cells such as sperm, neutrophils and retinal tissue (Pasantes-Morales *et al*., 1972; Alvarez and Storey, 1983; Learn *et al*., 1990; Green *et al*., 1991; Holmes *et al*., 1992) would reflect the turnover of hypotaurine *via* oxidative reactions and might be viewed as an indirect measure of the oxidative stress associated with such tissues. However, the mechanism of the oxidative reaction of the sulfinic group is not yet clearly defined. Recently, it has been shown that, besides nonspecific oxidants such as UV irradiation, hypochlorite, hydroxyl radical and photochemically generated singlet oxygen, also peroxynitrite mediates the oxidation of both hypotaurine and cysteine sulfinic acid to taurine and cysteic acid, respectively (Ricci *et al*., 1978; Green *et al*., 1985; Fellman *et al*., 1987; Pecci *et al*., 1999; Fontana *et al*., 2005). These findings have been related to the proposed role of hypotaurine as an antioxidant and free radical trapping agent *in vivo* (Aruoma *et al*., 1988; Tadolini *et al*., 1995). According to this, hypotaurine and cysteine sulfinic acid are able to prevent peroxynitrite-mediated reactions such as tyrosine nitration, α_1-antiproteinase inactivation and low-density lipoprotein oxidative modification (Fontana *et al*., 2004).

Peroxynitrite is a strong oxidizing and nitrating agent, which can be produced by the reaction of nitric oxide with superoxide anion (Koppenol *et al*., 1992; Huie and Padmaja, 1993; Pryor and Squadrito, 1995) and represents a reactive toxic species that can mediate cellular and tissue damage in various human diseases, including neurodegenerative disorders, inflammatory and autoimmune diseases (Eiserich *et al*., 1998; Stewart and Heales, 2003). At physiological pH both peroxynitrite anion ($ONOO^-$) and its conjugate

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* Dedicated to Professor Doriano Cavallini (1916-2005).

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acid (ONOOH, $pK_a = 6.8$) are present. Peroxynitrite is quite stable but upon protonation to peroxynitrous acid; it decays rapidly ($t_{1/2} < 1$ s) generating nitrate together with highly oxidizing and nitrating reactive species. It has been reported that peroxynitrite can oxidize suitable substrates, either through a direct one- or two-electron mechanism or by an indirect one-electron reaction involving hydroxyl ($^{\bullet}OH$) and nitrogen dioxide ($^{\bullet}NO_2$) radicals released during peroxynitrite homolysis (Radi *et al*., 2001).

In a recent work, the reaction of the sulfinates, hypotaurine and cysteine sulfinic acid with peroxynitrite has been shown to be associated with extensive oxygen uptake, suggesting that hypotaurine and cysteine sulfinic acid are oxidized by one-electron transfer mechanism to sulfonyl radicals which are converted to sulfonates by further oxygen-dependent reactions (Fontana *et al*., 2005). Beside the one-electron mechanism, hypotaurine and cysteine sulfinic acid can be oxidized by the two-electron pathway leading to direct sulfonate formation without oxygen consumption. The oxidation of sulfinates by peroxynitrite may thereby occur via the two reaction pathways.

In order to evaluate the mechanisms of oxidation of sulfinates by peroxynitrite and the relevance of the one- and the two-electron oxidative pathways, we compared oxygen consumption and sulfonate production at various concentrations of the two sulfinates. Peroxynitrite decomposition produces nitrate as main product while after reaction with a target molecule nitrite, whose quantity depends on the pathway of the oxidative reaction, is formed (Kissner and Koppenol, 2002; Jourd'heuil *et al*., 2003). Therefore, the amount of nitrite and nitrate formed in the reaction of peroxynitrite with hypotaurine and cysteine sulfinic acid at different pH has been also determined.

2. MATERIALS AND METHODS

2.1. Chemicals

Cysteine sulfinic acid, cysteic acid, hypotaurine, taurine were obtained from Sigma Chem Co. Diethylenetriamine pentaacetic acid (DTPA), tetrabutylammonium bisulfate, *o*-phthaldialdehyde and manganese dioxide were from Fluka. All other reagents were of the highest purity commercially available.

Peroxynitrite was synthesized from potassium nitrite and hydrogen peroxide under acidic conditions as previously described (Beckman *et al*., 1994), and excess hydrogen peroxide was removed by treatment with granular manganese dioxide. Typical peroxynitrite concentration after freeze fractionation was 600-700 mM as determined by absorbance at 302 nm using a molar absorption coefficient of 1670 $M^{-1}cm^{-1}$. Stock solutions of peroxynitrite were diluted with 0.1 M NaOH immediately before use to achieve the desired concentration.

2.2. Reaction of Hypotaurine or Cysteine Sulfinic Acid With Peroxynitrite

The reaction mixture contained hypotaurine or cysteine sulfinic acid at appropriate concentrations in 0.2 M phosphate buffer at pH 7.4 or 5.5. To avoid metal-catalyzed oxidative reactions, all samples contained 0.1 mM DTPA. The reaction was started by addition of peroxynitrite at a final concentration of 0.2 mM. To control for nonspecific effects of contaminating substances present in the peroxynitrite solutions or to stable peroxynitrite-decomposition products (nitrite and nitrate), peroxynitrite was first incubated

in phosphate buffer/DTPA for 10 min before the addition of hypotaurine or cysteine sulfinic acid (reverse order addition).

2.3. Oxygen Uptake

Oxygen uptake was performed using a Gilson 5/6 oxygraph and measured with a Clark type electrode in a water-jacketed cell (1.8 ml) at 25°C. The saturation oxygen concentration at this temperature was taken as 235 μM.

2.4. HPLC Analysis

Hypotaurine, cysteine sulfinic acid, taurine and cysteic acid were determined by high performance liquid chromatography (HPLC) using the *o*-phthaldialdehyde reagent (Hirschberger *et al*., 1985). Analyses were carried out with a Waters Chromatograph equipped with a Perkin-Elmer model LS-1 LC fluorescence detector using a 340-nm filter for excitation with an emission wavelength of 450 nm. The column was a 250 x 4.6 mm I.D. Simmetry C_{18}, 5 μm (Waters). The mobile phases were (A) 0.05 M sodium acetate (pH 5.5)-metanol (80:20, v/v) and (B) 0.05 M sodium acetate (pH 5.5)-metanol (20:80, v/v). The elution gradient was linear from A to 50% B in 5 min followed by isocratic at 50% B. Flow rate was 1 ml/min at room temperature. The elution times of cysteic acid, cysteine sulfinic acid, taurine and hypotaurine were 7.5, 10.5, 24.5, and 26 min, respectively.

Nitrite and nitrate were analyzed by ion-pairing HPLC as described previously (Jourd'heuil *et al*., 2003). Samples were injected onto a 250 x 4.6 mm I.D. Atlantis C_{18}, 5 μm (Waters) isocratically running at a flow rate of 1 ml/min with 10 mM K_2HPO_4, 10 mM tetrabutylammonium bisulfate in water-acetonitrile (95:5, v/v, pH 7). Detection was made at 210 nm using a Waters 996 photodiode array detector. The elution times of nitrite and nitrate were 8.5 and 20.5 min, respectively.

2.5. Statistical Analysis

Results are expressed as mean values ± SEM of at least three separate experiments. Graphics and data analysis were performed using GraphPad Prism 4 software.

3. RESULTS AND DISCUSSION

3.1. Peroxynitrite-Mediated Oxidation of Hypotaurine and Cysteine Sulfinic Acid

The oxidation of the sulfinates, hypotaurine and cysteine sulfinic acid, by peroxynitrite has been evaluated by monitoring the oxygen consumption and the production of the corresponding sulfonates, taurine and cysteic acid, at physiological pH.

When peroxynitrite is added to a solution containing the sulfinates (RSO_2^-), fast oxygen consumption is observed, suggesting the generation of intermediate radicals which react with oxygen. It is therefore proposed that the peroxynitrite-mediated oxidation of sulfinates probably involves an initial one-electron transfer mechanism with generation of sulfonyl radical ($RSO_2^{\bullet}$). Despite the controversial aspect of peroxynitrite chemistry, presently most investigators agree that one-electron oxidation is not a direct

reaction of peroxynitrite but depends on the interaction of the target molecule with the nitrogen dioxide ($^{\bullet}NO_2$) and hydroxyl radicals ($^{\bullet}OH$) released during the degradation process of peroxynitrite (Radi *et al*., 2001). According to this, the sulfinates can be indirectly oxidized to sulfonyl radicals by the peroxynitrite-derived free radicals:

$$RSO_2^- + {}^{\bullet}OH/{}^{\bullet}NO_2 \rightarrow RSO_2^{\bullet} + OH^-/NO_2^- \quad (1)$$

HPLC analyses of the incubation mixtures at the end of the reaction show that hypotaurine and cysteine sulfinic acid are oxidized to the corresponding sulfonates, taurine and cysteic acid.

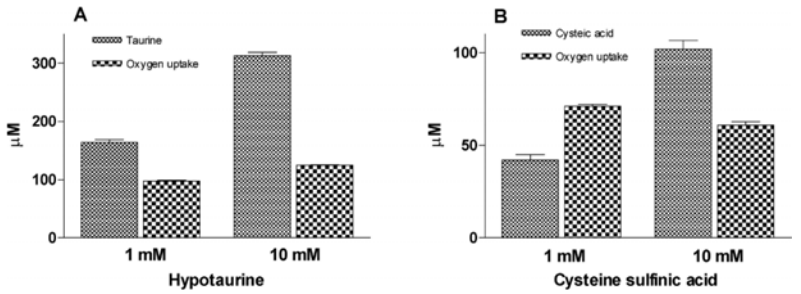


Figure 1. Oxidation of hypotaurine and cysteine sulfinic acid by peroxynitrite at pH 7.4. Peroxynitrite (200 µM) was added into the oxygraph chamber at 25°C, containing (1 or 10 mM) hypotaurine (A) or cysteine sulfinic acid (B) in 0.2 M phosphate buffer and 0.1 mM DTPA, pH 7.4, and the O_2 consumption was recorded. The reaction mixtures were subsequently analyzed by HPLC.

Fig. 1A shows oxygen uptake and the amount of taurine produced after the addition of 200 µM peroxynitrite to 1 mM and 10 mM hypotaurine at pH 7.4. It can be observed that at 10 mM hypotaurine, the amount of taurine produced is higher than the concentration of peroxynitrite added, evidencing the occurrence of a chain reaction mechanism responsible of amplification of the oxidation. Furthermore, the results show that the amount of oxygen consumed per mol of sulfonate produced is much lower at 10 mM hypotaurine.

Fig. 1B shows oxygen uptake and the amount of cysteic acid produced by reacting cysteine sulfinic acid with peroxynitrite in the same experimental condition as above. It can be observed: (a) at 1 mM cysteine sulfinc acid concentration, the amount of oxygen uptake is much higher than cysteic acid produced; (b) at 10 mM cysteine sulfinic acid, the amount of oxygen uptake is lower than at 1 mM cysteine sulfinic acid; and (c) the yields of cysteic acid are lower when compared to taurine obtained after the reaction of peroxynitrite with hypotaurine under the same reaction conditions. These results can be explained by the already reported tendency of cysteine sulfinic acid-derived radical to decompose sulfur dioxide (SO_2) produced and a carbon-centered radical ($R^{\bullet}$) (Harman *et al*., 1984). Subsequent oxidation of sulfite (aqueous sulfur dioxide) to sulfate involves additional free radical mechanisms leading to oxygen consumption (Mottley and Mason, 1988; Karoui *et al*., 1996). The previously reported detection of sulfate in the incubation mixtures of cysteine sulfinic acid with peroxynitrite indicates that cysteine sulfinic acid-

derived sulfonyl radical undergoes a significative decomposition at physiological pH 7.4 (Fontana *et al*., 2005). Accordingly, the high oxygen uptake, observed during the reaction of cysteine sulfinic acid with peroxynitrite, can account, in addition to that required for oxidation of cysteine sulfinic acid to cysteic acid, for the oxidation of sulfite to sulfate. It is also possible that the high reactive alkyl radical ($R^{\bullet}$) can react with oxygen, contributing to the observed oxygen uptake. Interestingly, compared to the cysteine sulfinic acid-derived sulfonyl radical, the sulfonyl radical derived from the oxidation of hypotaurine appears to have a much lower tendency to decompose as indicated by the finding that the amount of oxygen consumed per mole of taurine produced is much lower than that observed in the oxidation of cysteine sulfinic acid.

The oxidative reactions mediated by peroxynitrite are expected to take place by both one- and two-electron mechanisms (Radi *et al*., 2001). As mentioned above, it is recognized that the one-electron mechanism is not a direct reaction of peroxynitrite but depends on the radicals $^{\bullet}OH$ and $^{\bullet}NO_2$ derived from peroxynitrite decomposition. In the two-electron mechanism, peroxynitrite reacts directly with the target molecule in an overall second-order process. Although the observed oxygen consumption associated with oxidation of sulfinates by peroxynitrite indicates a relevant contribution of the one-electron pathway, the two-electron mechanism could represent an additional route of oxidation of sulfinates leading to direct sulfonate formation without oxygen consumption.

The results that the oxygen consumed per mole of sulfonate produced decreases considerably with the increase of sulfinate concentration, indicate that the reaction may occur *via* the two mechanisms whose relative importance depends on reagent concentrations. At 1 mM RSO_2^- concentration, where the oxygen uptake associated with the oxidation of sulfinates is higher; the one-electron mechanism with the intermediate formation of sulfonyl radicals is likely to predominate. In this case, the radicals $^{\bullet}OH$ and $^{\bullet}NO_2$ produced during peroxynitrite decomposition oxidize RSO_2^- to $RSO_2^{\bullet}$ radicals which are responsible of oxygen consumption. Additionally, the formation of sulfonyl radicals initiates an oxygen-dependent radical chain reaction that could greatly amplify the importance of the one-electron pathway. At 10 mM RSO_2^- concentrations the oxygen uptake associated with the oxidation of sulfinates decreases, as the second-order reaction of the two sulfinates with peroxynitrite becomes more significant. In this pathway, peroxynitrite participates as two-electron oxidant and will oxidize the sulfinates without the formation of sulfonyl radicals, and thus with no associated oxygen consumption (see Scheme 1).

3.2. Effect of pH on the Interaction of Peroxynitrite With Sulfinates

To evaluate the effect of pH on peroxynitrite-mediated oxidation of sulfinates, we monitored hypotaurine and cysteine sulfinic acid oxidation at pH 5.5 by sulfonate production and oxygen consumption. The data presented in Fig. 2 show that in the reaction of 1 mM sulfinates with 200 μM peroxynitrite at acidic pH, the yields of representive sulfonates are greater than those at pH 7.4. These data suggest that peroxynitrous acid (ONOOH, pK_a = 6.8) is the reactive species. Kinetic experiments performed at various pH are consistent with this interpretation (Fontana *et al*., 2005).

The oxygen uptake associated with the reaction carried out at pH 5.5 reveals a stoichiometry of approximately 0.5 mol of oxygen consumed per mol of sulfonate produced. These results indicate that at acidic pH, the cysteine sulfinic acid-derived sulfonyl radical appears to have a lower tendency to decompose.

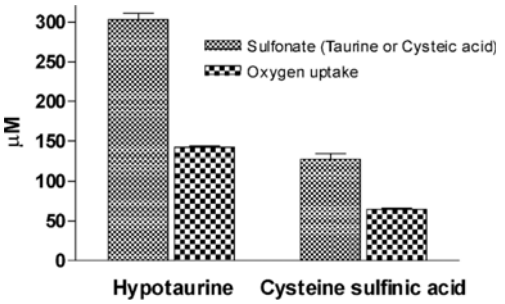


Figure 2. Oxidation of hypotaurine and cysteine sulfinic acid by peroxynitrite at pH 5.5. Peroxynitrite (200 µM) was added into the oxygraph chamber at 25°C, containing 1 mM hypotaurine (A) or 1 mM cysteine sulfinic acid (B) in 0.2 M phosphate buffer and 0.1 mM DTPA, pH 5.5, and the O_2 consumption was recorded. The reaction mixtures were subsequently analyzed by HPLC.

3.3. Measurement of Nitrite and Nitrate During the Oxidation of Sulfinates by Peroxynitrite

In the two-electron process of oxidation of sulfinate by peroxynitrite, nitrite and sulfonate would be the only products:

$$RSO_2^- + ONOO^-/ONOOH \rightarrow RSO_3^- + NO_2^- \quad (2)$$

If sulfinates are oxidized by one-electron mechanism, also nitrate will be formed. This is because the peroxynitrite-derived radicals $^{\bullet}OH$ and $^{\bullet}NO_2$, initially formed in a solvent cage, undergo rapid recombination to form nitrate (about 70%) or escape the cage (about 30%) to give free radicals, which react with sulfinates (Mottley and Mason, 1988; Karoui *et al.,* 1996). Thus, the product distribution of nitrite and nitrate can provide a further mean to establish the contribution of the two pathways.

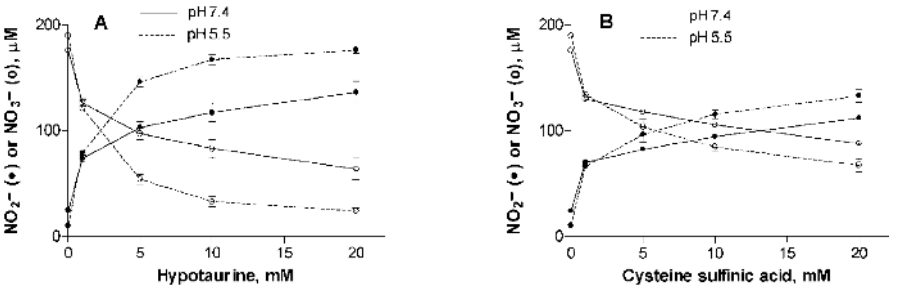
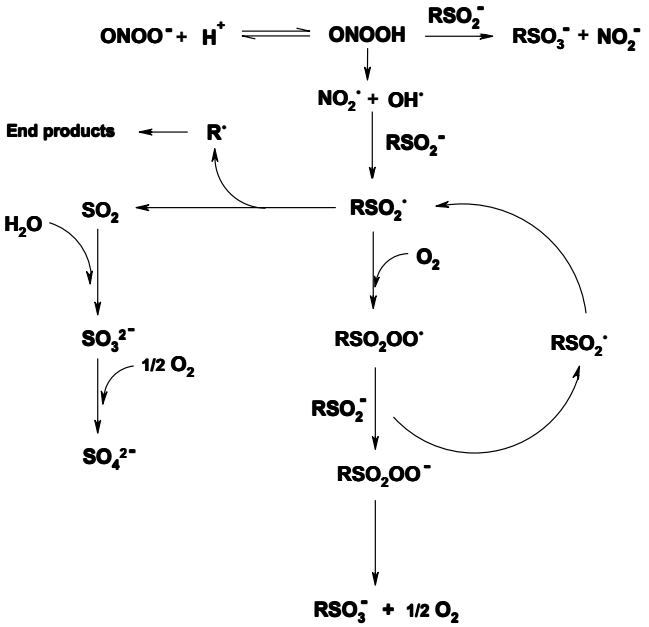


Figure 3. Oxidation of hypotaurine and cysteine sulfinic acid by peroxynitrite: nitrite and nitrate formation. Peroxynitrite (200 µM) was incubated with different concentrations of hypotaurine (A) and cysteine sulfinic acid (B), in 0.2 M phosphate buffer containing 0.1 mM DTPA at room temperature for 15 min, followed by the determination of NO_2^- and NO_3^-.

The concentrations of nitrite and nitrate formed during the decomposition of the peroxynitrite at pH 7.4 and 5.5 in the presence of various concentrations of sulfinates are reported in Fig. 3. The increase of nitrite and the decrease of nitrate formed during the reaction of 200 μM peroxynitrite with increasing concentrations of sulfinates further support the conclusion that the two pathways coexist and that the direct reaction (i.e., two-electron oxidation) would prevail quantitatively over the one-electron oxidation when sulfinates are present in large excess over peroxynitrite. The unexpected low yield of nitrite observed in the reaction of peroxynitrite with cysteine sulfinic acid could be explained by a partial reoxidation of produced nitrite by secondary radicals generated by decomposition of the cysteine sulfinic acid-derived sulfonyl radicals.

4. CONCLUSION

The data presented in this work demonstrate that the sulfinates (RSO_2^-), hypotaurine and cysteine sulfinic acid are oxidized by peroxynitrite to form the corresponding sulfonates (RSO_3^-), taurine and cysteic acid. The data demonstrate that the peroxynitrite-mediated oxidation of sulfinates may occur either through one- or two-electron pathways whose relative importance depends on reagent concentrations and pH. We propose that one-electron oxidation, mediated by the peroxynitrite-derived free radicals, produces sulfonyl radicals ($RSO_2^{\bullet}$) as intermediates. The peroxynitrite-mediated oxidative pathways of sulfinates are shown in the scheme 1.



Scheme 1. Oxidative pathways of sulfinates.

The consumption of oxygen by the peroxynitrite-dependent oxidation of sulfinates could result from the known reaction of sulfonyl radicals with oxygen with production of sulfonyl peroxyl radical ($RSO_2OO^{\bullet}$) (Sevilla *et al*., 1990). The sulfonyl peroxyl radical is a highly reactive intermediate (Sevilla *et al*., 1990) and its possible reaction with excess sulfinate can proceed to give peroxysulfonate (RSO_2OO^{-}). The peroxysulfonate formed would decompose to give sulfonate and molecular oxygen.

It should be noted that sulfonyl radicals, as shown in the scheme, may initiate an oxygen-dependent radical chain propagation step that could be responsible of amplification of the oxidation.

Other possible reactions previously suggested for sulfonyl radical (Fellman *et al*., 1987; Green and Fellman, 1994) include its dimerization to form the corresponding disulfone ($RSO_2–SO_2R$) and its condensation with the sulfonyl peroxyl radical intermediate leading to the persulfonate ($RSO_2–OO–SO_2R$). Subsequent hydrolysis of the disulfone or of the persulfonate could represent additional routes for the production of sulfonates:

$$RSO_2–SO_2R + H_2O \rightarrow RSO_2^{-} + RSO_3^{-} + 2H^{+} \quad (3)$$

$$RSO_2–OO–SO_2R + H_2O \rightarrow 2\,RSO_3^{-} + ½\,O_2 + 2H^{+} \quad (4)$$

However, the production of sulfonates through the intermediate formation of disulfone do not require oxygen, in contrast with the observed oxygen consumption associated with the oxidative reaction.

In conclusion, the above results indicate that peroxynitrite and its derived species can be included into the non-specific biological oxidant able to accomplish the oxidation of the sulfinic group of hypotaurine and cysteine sulfinic acid to the sulfonic of taurine and cysteic acid, respectively. However, the formation of intermediate sulfonyl radicals, which can propagate oxidative reactions, raises the question about the metabolic fate and/or the pathophysiological significance of these species. Among sulfur-centered radicals, it has been already shown that thiyl radicals ($RS^{\bullet}$), generated by one-electron oxidation of thiols, react with molecular oxygen to form thiyl peroxyl radical ($RSOO^{\bullet}$) which can rearrange to sulfonyl radical ($RSO_2^{\bullet}$) that further react with oxygen to generate the sulfonyl peroxyl radical ($RSO_2OO^{\bullet}$) (Sevilla *et al*., 1990). Both thiyl and thiyl-derived radicals such as sulfonyl radical are potent initiators of lipid peroxidation (Schöneich *et al*., 1992), thus behaving as oxidants, which can exert damaging effects *in vivo*. However, the biological relevance of $RS^{\bullet}$-derived radicals remains a matter of debate and recently an additional group of redox active molecules termed reactive sulfur species (RSS) has been proposed to be formed *in vivo* under conditions of oxidative stress (Giles *et al*., 2001). Although sulfur-containing molecules are generally considered to act as antioxidants and, in particular, our previous studies showed that hypotaurine and cysteine sulfinic acid have the ability to inhibit peroxynitrite-dependent reactions (Fontana *et al*., 2004), the transient formation of sulfur reactive species during the oxidative reaction, could have a physiological importance which remain to be investigated.

5. REFERENCES

Alvarez, J. G. and Storey, B. T., 1983, Taurine, hypotaurine, epinephrine and albumin inhibit lipid peroxidation in rabbit spermatozoa and protect against loss of motility, *Biol. Reprod.* **29**:548.

Aruoma, O. I., Halliwell, B., Hoey, B. M., and Butler, J., 1988, The antioxidant action of taurine, hypotaurine and their metabolic precursor, *Biochem. J.* **256**:251.

Augusto, O., Bonini, M. G., Amanso, A. M., Linares, E., Santos, C. C. X., and De Menezes, S. L., 2002, Nitrogen dioxide and carbonate radical anion: two emerging radicals in biology, *Free Radic. Biol. Med.* **32**:841.

Beckman, J. S., Chen, J., Ischiropoulos, H., and Crow, J. P., 1994, Oxidative chemistry of peroxynitrite, *Methods Enzymol.* **233**:229.

Eiserich, J. P., Patel, R. P., and O'Donnel, V. B., 1998, Pathophysiology of nitric oxide and related species: free radical reactions and modification of biomolecules, *Mol. Aspects Med.* **19**:221.

Fellman, J. H., Green, T. R., and Eicher, A. L., 1987, The oxidation of hypotaurine to taurine: bis-aminoethyl-α-disulfone, a metabolic intermediate in mammalian tissue, *Adv. Exp. Med. Biol.* **217**:39.

Fontana, M., Pecci, L., Duprè, S., and Cavallini, D., 2004, Antioxidant properties of sulfinates: protective effect of hypotaurine on peroxynitrite-dependent damage, *Neurochem. Res.* **29**:111.

Fontana, M., Amendola, D., Orsini, E., Boffi, A., and Pecci, L., 2005, Oxidation of hypotaurine and cysteine sulphinic acid by peroxynitrite, *Biochem. J.* **389**:233.

Giles, G. I., Tasker, K. M., and Jacob, C., 2001, Hypothesis: the role of reactive sulfur species in oxidative stress, *Free Radic. Biol. Med.* **31**:1279.

Green, T. R., Fellman, J. H., and Eicher, A. L., 1985, Myeloperoxidase oxidation of sulfur-centered and benzoic acid hydroxyl radical scavengers, *FEBS Lett.* **192**:33.

Green, T. R., Fellman, J. H., Eicher, A. L., and Pratt, K. L., 1991, Antioxidant role and subcellular location of hypotaurine and taurine in human neutrophils, *Biochim. Biophys. Acta* **1073**:91.

Green, T. R. and Fellman, J. H., 1994, Effect of photolytically generated riboflavin radicals and oxygen on hypotaurine antioxidant free radical scavenging activity, *Adv. Exp. Med. Biol.* **359**:19.

Harman, L. S., Mottley, C., and Mason, R. P., 1984, Free radical metabolites of L-cysteine oxidation, *J. Biol. Chem.* **259**:5609.

Hirschberger, L. L., De la Rosa, J., and Stipanuk, M., 1985, Determination of cysteinesulfinate, hypotaurine and taurine in physiological samples by reversed-phase high-performance liquid chromatography, *J. Chromatogr. B* **343**:303.

Holmes, R. P., Goodman, H. O., Shihabi, Z. K., and Jarow, J. P., 1992, The taurine and hypotaurine content of human semen, *J. Androl.* **13**:289.

Huie, R. E. and Padmaja, S., 1993, The reaction of NO with superoxide, *Free Rad. Res. Commun.* **18**:195.

Huxtable, R. J., 1992, Physiological actions of taurine, *Physiol. Rev.* **72**:101.

Jourd'heuil, D., Jourd'heuil, F. L., and Feelisch, M., 2003, Oxidation and nitrosation of thiols at low micromolar exposure to nitric oxide. Evidence for a free radical mechanism, *J. Biol. Chem.* **278**:15720.

Karoui, H., Hogg, N., Fréjaville, C., Tordo, P., and Kalyanaraman, B., 1996 Characterization of sulfur-centered radical intermediates formed during the oxidation of thiols and sulfite by peroxynitrite. ESR-spin trapping and oxygen uptake studies, *J. Biol. Chem.* **271**:6000.

Kissner, R., and Koppenol, W. H., 2002, Product distribution of peroxynitrite decay as function of pH, temperature, and concentration, *J. Am. Chem. Soc.* **124**:234.

Koppenol, W. H., Moreno J. J., Pryor W. A., Ischiropoulos H., and Beckman, J. S., 1992, Peroxynitrite, a cloaked oxidant formed by nitric oxide and superoxide, *Chem. Res. Toxicol.* **5**:834.

Learn, D. B., Fried, V. A., and Thomas, E. L., 1990, Taurine and hypotaurine content of human leukocytes, *J. Leukoc. Biol.* **48**:174.

Mottley, C. and Mason, R. P., 1988, Sulfate anion radical formation by the peroxidation of (bi)sulfite and its reaction with hydroxyl radical scavengers, *Arch. Biochem. Biophys.* **267**:681.

Pasantes-Morales, H., Klethi, J., Ledig, M., and Mandel, P., 1972, Free amino acids of chicken and rat retina, *Brain Res.* **41**:494.

Pecci, L., Costa, M., Montefoschi, G., Antonucci, A., and Cavallini, D., 1999, Oxidation of hypotaurine to taurine with photochemically generated singlet oxygen: the effect of azide, *Biochem. Biophys. Res. Commun.* **254**:661.

Pryor, W. A. and Squadrito, G. L., 1995, The chemistry of peroxynitrite: a product from the reaction of nitric oxide with superoxide, *Am. J. Physiol.* **268**:L699.

Radi, R., Peluffo, G., Alvarez, M. N., Naviliat, M., and Cayota, A., 2001, Unraveling peroxynitrite formation in biological system, *Free Radic. Biol. Med.* **30**:463.

Ricci, G., Duprè, S., Federici, G., Spoto, G., Matarese, R. M., and Cavallini, D., 1978, Oxidation of hypotaurine to taurine by ultraviolet irradiation, *Physiol. Chem. Phys.* **10**:435.

Schöneich, C., Dillinger, U., von Bruchhausen, F., and Asmus, K.-D., 1992, Oxidation of polyunsaturated fatty acids and lipids through thiyl and sulfonyl radicals: reaction kinetics, and influence of oxygen and structure of thiyl radicals, *Arch. Biochem. Biophys.* **292**:456.

Sevilla, M. D., Becker, D., and Yan, M., 1990, The formation and structure of the sulfoxyl radicals $RSO^{\bullet}$, $RSOO^{\bullet}$, $RSO_2^{\bullet}$, and $RSO_2OO^{\bullet}$ from the reaction of cysteine, glutathione and penicillamine thiyl radicals with molecular oxygen, *Int. J. Radiat. Biol.* **57**:65.

Stewart, V. C. and Heales, S. J., 2003, Nitric oxide-induced mitochondrial dysfunction: implications for neurodegeneration, *Free Radic. Biol. Med.* **34**:287.

Tadolini, B., Pintus, G., Pinna, G. G., Bennardini, F., and Franconi, F., 1995, Effects of taurine and hypotaurine on lipid peroxidation, *Biochem. Biophys. Res. Commun.* **213**:820.

Wright, C. E., Tallan, H. H., Lin, Y. Y., and Gaull, G. E., 1986, Taurine: biological update, *Annu. Rev. Biochem.* **55**:427.

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