Reactivity of Hydrogen Sulfide Towards Disulfides and Sulfenic Acids

Cuevasanta, E.[1], Ferrer-Sueta, G.[2], Alvarez B.[1]

[1]Laboratorio de Enzimología and [2]Laboratorio de Fisicoquímica Biológica, Facultad de Ciencias, Universidad de la República, Montevideo, Uruguay

Introduction: In contrast to its classical conception as a highly toxic gas, hydrogen sulfide (H_2S) is now being considered a physiological modulator in mammals. However, the molecular bases of its effects are not fully understood. The reaction of hydrogen sulfide with disulfides (RSSR) and sulfenic acids (RSOH) to form persulfides (RSSH) could constitute a possible mechanism. **Objectives:** To better understand the reactions of hydrogen sulfide towards disulfides and sulfenic acids. **Materials and Methods:** Kinetic characterization of reactions of H_2S with disulfides and sulfenic acid. **Results and Discussion:** We studied the reactivity of hydrogen sulfide towards symmetrical low molecular weight (LMW) disulfides and mixed disulfides formed between cysteine 34 of human serum albumin (HSA) and LMW thiols. The second-order rate constants obtained for the six symmetric disulfides studied are lower than those reported for alkyl thiols. The reduction of disulfides by the hydrosulfide anion seemed to occur through a concerted mechanism, producing a thiolate (leaving group) and a persulfide (RSSH). Brønsted correlations between the pH-independent rate constants and the pK_as of the different leaving thiols were obtained and compared to thiol-disulfide exchange reactions. The reaction of hydrogen sulfide with the relatively stable sulfenic acid that is formed in HSA (HSA-SOH) was investigated using an experimental design involving competition between hydrogen sulfide and thiols for HSA-SOH. We determined the second-order rate constant of this reaction as $(2.7 \pm 0.8) \times 10^2$ M^{-1} s^{-1} (pH 7.4, 25 ºC). These reactions lead to the formation of persulfides. The reactivity of the persulfide in HSA (HSA-SSH) was kinetically evaluated and showed a 20-fold increased reactivity towards dithiopyridine compared to the parent thiol. This increase can be rationalized by the alpha effect. **Conclusions:** This study contributes to the understanding of how the reactions of H_2S with oxidized thiol derivatives to form persulfides could constitute plausible ways of unleashing physiological responses.

This work was supported by L'Oréal-UNESCO, PEDECIBA and ANII, Uruguay.