

## Supplementary Materials

### Sulfide ( $\text{Na}_2\text{S}$ ) and polysulfide ( $\text{Na}_2\text{S}_2$ ) interacting with doxycycline produce/scavenge superoxide and hydroxyl radicals and induce/inhibit DNA cleavage

Anton Misak<sup>1</sup>, Lucia Kurakova<sup>2</sup>, Eduard Goffa<sup>3</sup>, Vlasta Brezova<sup>4</sup>, Marian Grman<sup>1</sup>, Elena Ondriasova<sup>2</sup>, Miroslav Chovanec<sup>3</sup> and Karol Ondrias<sup>1</sup>

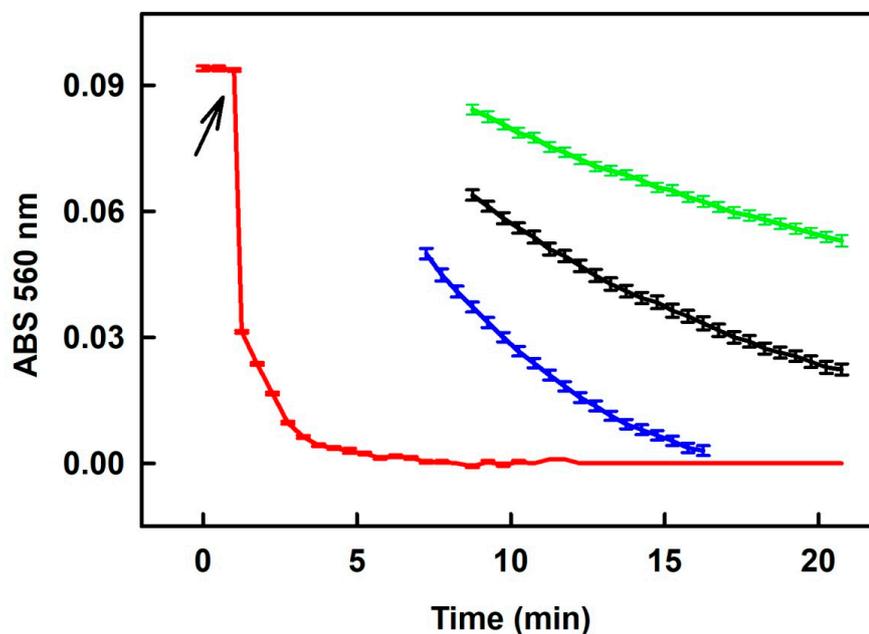
<sup>1</sup> Institute of Clinical and Translational Research, Biomedical Research Center, University Science Park for Biomedicine, Slovak Academy of Sciences, 845 05 Bratislava, Slovak Republic

<sup>2</sup> Department of Pharmacology and Toxicology, Faculty of Pharmacy, Comenius University, 832 32 Bratislava, Slovak Republic

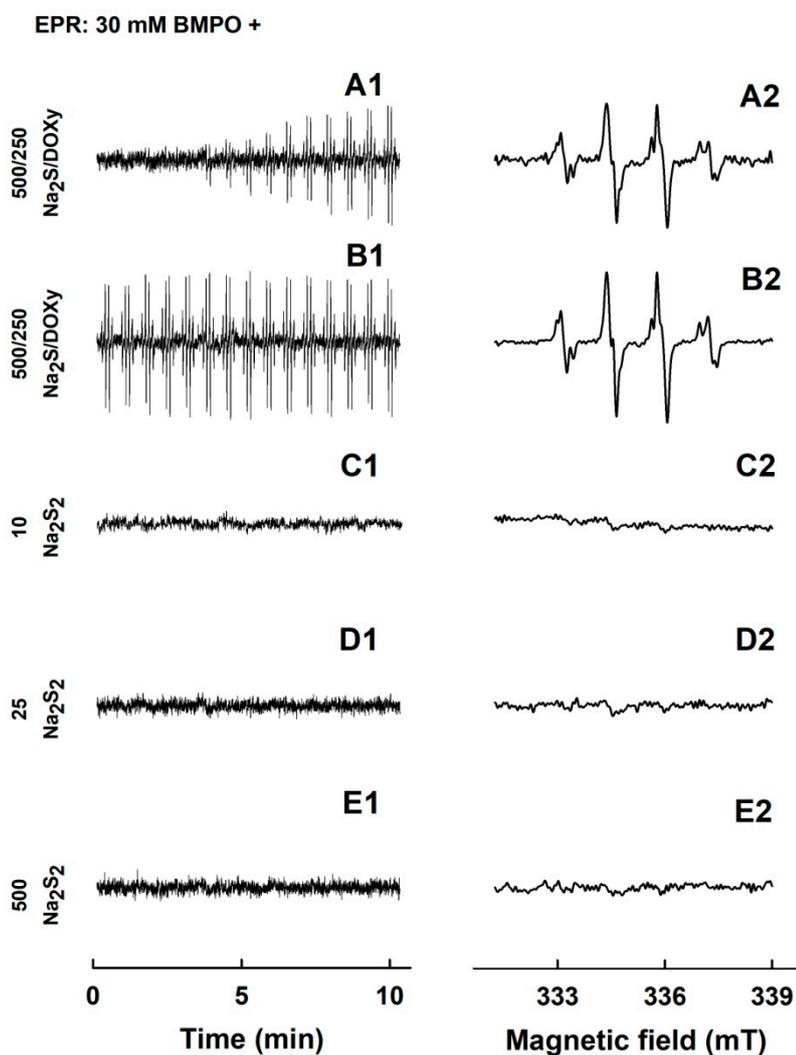
<sup>3</sup> Cancer Research Institute, Biomedical Research Center, University Science Park for Biomedicine, Slovak Academy of Sciences, 845 05 Bratislava, Slovak Republic

<sup>4</sup> Faculty of Chemical and Food Technology, Slovak University of Technology, 812 37 Bratislava, Slovak Republic

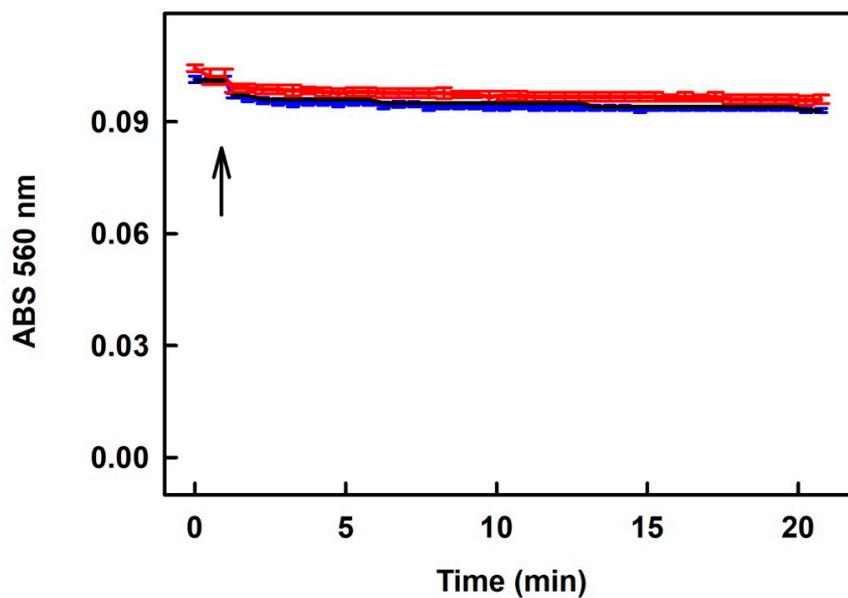
Correspondence: karol.ondrias@savba.sk, Tel.:+421-908577943



**Figure S1.** Time-dependent reduction of the \*cPTIO radical by  $\text{Na}_2\text{S}_3$ . Reduction of the \*cPTIO radical was detected as the decrease of ABS at 560 nm minus ABS at 730 nm (ABS 560 nm). Arrow indicates addition of  $100 \mu\text{M}$  \*cPTIO to  $100 \mu\text{M}$   $\text{Na}_2\text{S}_3$  incubated 15 s (red), 20 min (blue), 40 min (black) and 70 min (green) in the buffer consisting of 100 mM sodium phosphate and  $100 \mu\text{M}$  DTPA pH 7.4, at  $37^\circ\text{C}$ . Means  $\pm$  SE;  $n = 3$ . Due to difficulties of background subtraction, the first (7-10 min) data for 20, 40 and 70 min incubation are not available.



**Figure S2.** EPR spectra of the  $\bullet$ BMPO adducts for  $\text{Na}_2\text{S}_2$ ,  $\text{Na}_2\text{S}$  and DOXY and their mutual combinations. The sets of individual EPR spectra of the  $\bullet$ BMPO adducts were monitored in 15 sequential scans, each 42 s (**A1-E1**), starting  $110 \pm 15$  s after sample preparation. Fifteen EPR spectra were accumulated (**A2-E2**). The samples containing 30 mM  $\bullet$ BMPO with 500/250  $\mu\text{M}/\mu\text{M}$   $\text{Na}_2\text{S}/\text{DOXY}$  monitored in 15 sequential scans (**A1**) and the continuation of the recording further 15 sequential scans (**B1**) over the next 10 minutes.  $\bullet$ BMPO (30 mM) in the presence of 10 (**C1** and **C2**), 25 (**D1** and **D2**) and 500  $\mu\text{M}$   $\text{Na}_2\text{S}_2$  (**E1** and **E2**). The intensities of the time-dependent EPR spectra (**A1-E1**) and detailed spectra (**A2-E2**) are comparable as they were measured under identical EPR settings (except for the spectra **B2**, which was multiply by 0.5). EPR spectra of the  $\bullet$ BMPO spin-adducts were measured on a Bruker EMX spectrometer, X-band  $\sim 9.4$  GHz, 335.15 mT central field, 8 mT scan range, 20 mW microwave power, 0.1 mT modulation amplitude, 42 s sweep time, 20.48 ms time constant, and 20.48 ms conversion time at  $37^\circ\text{C}$ .



**Figure S3.** Time-dependent reduction of the  $\bullet$ cPTIO radical by the studied compounds. Reduction of the  $\bullet$ cPTIO radical was detected as decrease of ABS at 560 nm minus ABS at 730 nm (ABS 560 nm). Buffer: 100 mM sodium phosphate, 100  $\mu$ M DTPA, pH 7.4, at 37°C. Arrow indicates addition of fusaric acid (400  $\mu$ M, red) or norfloxacin (400  $\mu$ M, blue) and control 5% DMSO (black) to 100/400  $\mu$ M/ $\mu$ M  $\bullet$ cPTIO/ $\text{Na}_2\text{S}$ . Means  $\pm$  SE, n = 3.