Supporting Information

Self-cascade MoS$_2$ nanozymes for efficient intracellular antioxidation and hepatic fibrosis therapy

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Other Methods

Electron spin resonance measurements

All electron spin resonance (ESR) measurements were carried out at ambient temperature using a Bruker E500 ESR spectrometer.

Measurement of CAT-like activity. Electron spin resonance (ESR) spin label oximetry was employed to investigate the oxygen generation from H$_2$O$_2$ catalyzed by MoS$_2$ nanosheets at two pH levels. Sample solutions including 0.1 mM spin label $^{15}$N-PDT (Cambridge Isotope Labs, USA), 100 μg/mL MoS$_2$ nanosheets, and buffer solutions (pH 4.5 or 7.4) were deoxygenated with nitrogen before the initiation of reactions by addition of 1.0 mM H$_2$O$_2$. ESR spectral measurements were obtained using the following settings: 0.04 G field modulation, 3 G scan range, and 1 mW microwave power.

Measurement of SOD-like activity. To investigate the O$_2^•−$ scavenging ability of MoS$_2$ nanosheets, two O$_2^•−$ sources, xanthine-xanthine oxidase (XAN-XOD) and KO$_2$/18-crown-6-ether systems, were used to generate O$_2^•−$. BMPO (Dojindo Laboratories, Japan) was used to trap the O$_2^•−$ in the form of spin adduct BMPO/$•$OOH. ESR spectral measurements were obtained using the following settings: 1 G field modulation, 100 G scan range, and 20 mW microwave power.

Measurement of antioxidative effects of MoS$_2$ nanosheets through interaction with cytochrome c/H$_2$O$_2$. Oxidation of the spin trap DMPO (Dojindo Laboratories, Japan), to form 5,5-dimethyl-1-pyrrolidone-N-oxyl (DMPOX), was monitored by ESR to determine the effects of MoS$_2$ nanosheets on cytochrome c (Cyt c)’s ability to catalyze
the oxidation of substrates by H₂O₂. Time dependence of the ESR signal for the Cyt c/H₂O₂ system with MoS₂ nanosheets or PBS (control) was measured. ESR spectral measurements were obtained using the following settings: 1 G field modulation, 100 G scan range, and 10 mW microwave power.
Table S1 Michaelis-Menten parameters of MoS$_2$ nanosheets.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>$K_m$ (mM)</th>
<th>$V_{max}$ $(10^{-6}$ M s$^{-1}$)</th>
<th>$K_{cat}$ $(10^{-3}$ s$^{-1}$)</th>
<th>$K_{cat}/K_m$ $(10^{-3}$ mM$^{-1}$ s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H$_2$O$_2$</td>
<td>0.04</td>
<td>0.66</td>
<td>1.05</td>
<td>26.25</td>
</tr>
<tr>
<td>GSH</td>
<td>1.68</td>
<td>0.94</td>
<td>1.50</td>
<td>0.89</td>
</tr>
</tbody>
</table>
Fig. S1 (a) AFM and (b) SEM images of MoS$_2$ nanosheets.
Fig. S2 (a) The absorbance spectra of TMB oxidized by MoS$_2$ nanosheets. (b) Typical photographs of TMB reaction solutions oxidized by MoS$_2$ nanosheets in the presence of H$_2$O$_2$ under pH 4.5. (I) 1 mM H$_2$O$_2$ and 1 mM TMB; (II) 100 μg/mL MoS$_2$ nanosheets and 1 mM TMB; (III) 1 mM H$_2$O$_2$, 1 mM TMB and 100 μg/mL MoS$_2$ nanosheets.
Fig. S3 The quantification of (a) oxygen and (b) H$_2$O$_2$ production from superoxide turnover by MoS$_2$ nanosheets vs 1 U/mL SOD in KO$_2$/18-crown-6-ether system. ***$p < 0.001$ when compared with control group.
**Fig. S4** Corresponding double-reciprocal plots of MoS$_2$ nanosheets at a fixed concentration of one substrate *versus* varying the concentration of another for (a) H$_2$O$_2$ and (b) GSH.
**Fig. S5** Lowest-energy adsorption structures of the intermediate species during the H$_2$O$_2$ decomposition process on the basal plane of the MoS$_2$ nanosheets under neutral (top panel) and acidic (bottom panel) conditions (white, H; red, O; yellow, S; cyan, Mo).
Fig. S6 Lowest-energy adsorption structures of the intermediate species during the H$_2$O$_2$ decomposition process on the Mo-S-edge of the MoS$_2$ nanosheets under neutral (top panel) and acidic (bottom panel) conditions (white, H; red, O; yellow, S; cyan, Mo). Here, it is noteworthy that the adsorption of H$_2$O$_2$ on Mo-S-edge is a chemical dissociative adsorption.
**Fig. S7** Lowest-energy adsorption structures of the intermediate species during the H$_2$O$_2$ decomposition process on the S-edge of the MoS$_2$ nanosheets under neutral (top panel) and acidic (bottom panel) conditions (white, H; red, O; yellow, S; cyan, Mo).
Fig. S8 (a) Comparison between two stable adsorptions of $\text{H}^+$ on the Mo-edge; the adsorption at the H-site is more energetically stable. (b) Lowest-energy adsorption structures of the intermediate species during the $\text{H}_2\text{O}_2$ decomposition process on the Mo-edge of the MoS$_2$ nanosheets under neutral (top panel) and acidic (bottom panel) conditions (white, H; red, O; yellow, S; cyan, Mo).
Fig. S9 Blood hematology data of mice injected with saline (normal group) or MoS$_2$ nanosheets (0.5 mg/kg.bw) once a week for four weeks.