

## Supplementary Material

# A Review on Bioactive Anthraquinone and Derivatives as the Regulators for ROS

Lihua Zhao<sup>1</sup> and Lin Zheng<sup>2,\*</sup>

<sup>1</sup> Tianjin Renai College, Tianjin 301636, China; huazi.95@163.com

<sup>2</sup> College of Pharmaceutical Engineering of Traditional Chinese Medicine, Tianjin University of Traditional Chinese Medicine, Tianjin 301617, China

\* Correspondence: zhenglin@tjutcm.edu.cn

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**Figure S1.** The illustration of ROS formation. The symbols and abbreviations are as follows:  $\cdot\text{OH}$ , hydroxyl radical;  $\text{O}_2^{\cdot-}$ , superoxide radical;  $\text{H}_2\text{O}_2$ , hydrogen peroxide;  $\text{OH}^-$ , hydroxide anion; SOD, superoxide dismutase; CAT, catalase; GPX, glutathione peroxidase; GSH, reduced glutathione; GSSG, oxidized glutathione; GSR, glutathione reductase; GST, glutathione S-transferase.

**Figure S2.** Redox cycling of quinones and the effect of the different components. One-electron reduction ( $1e^-$ ) of the semiquinone undergoes aerobic oxidation [O] to generate  $\text{O}_2^{\cdot-}$  and the parent quinone. Under anaerobic conditions, the semiquinone could undergo a disproportionation reaction yielding quinone and the corresponding hydroquinone. Two-electron reduction ( $2e^-$ ) of quinone produces hydroquinone, which may undergo a compounding reaction with quinone to produce semiquinone that is oxidized to semiquinone and  $\text{O}_2^{\cdot-}$ , producing reactive alkylating agents and/or is excreted from the body. The semiquinones and  $\text{O}_2^{\cdot-}$  produced by the process eventually lead to oxidative stress and cell damage.

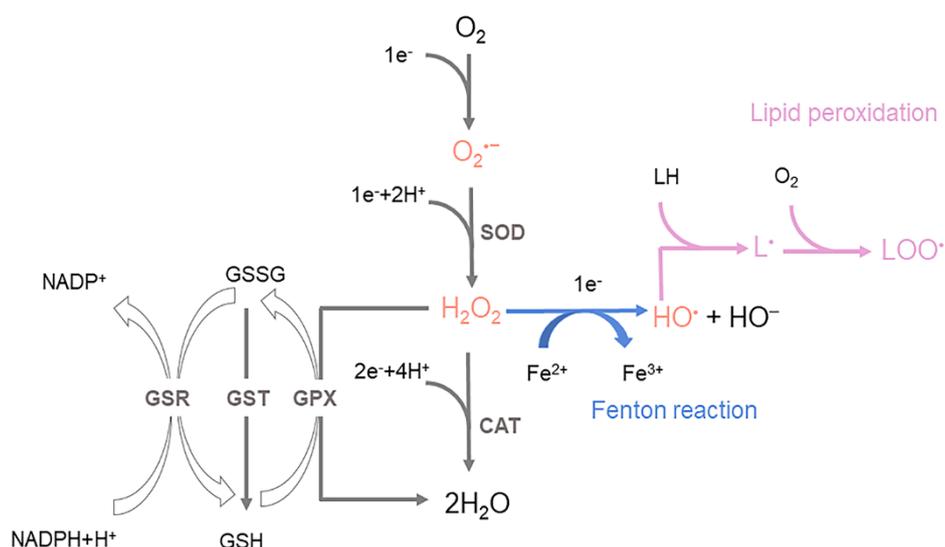
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**Table S2.** The BDE value of free radical species (1-OH, 3-OH, and 8-OH) of emodin (**1**).

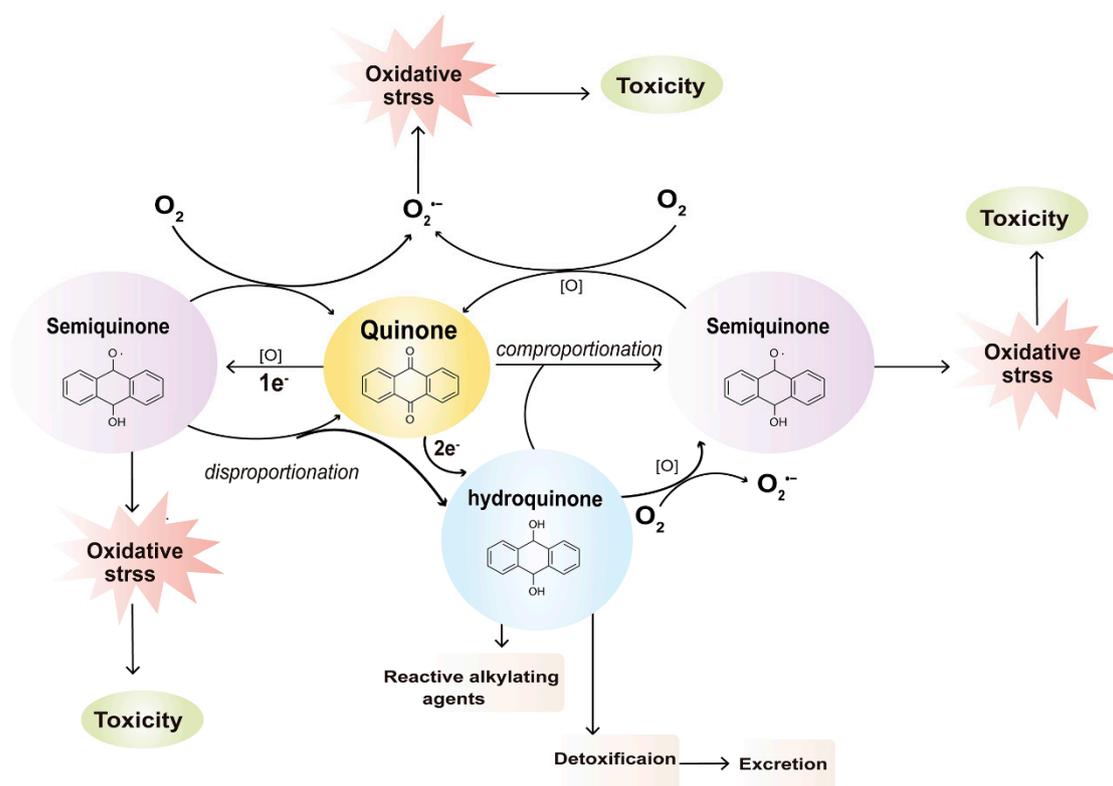
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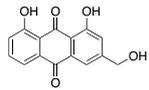
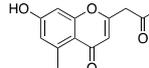
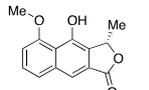


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**Figure S2.** Redox cycling of quinones and the effect of the different components. One-electron reduction ( $1e^-$ ) of the semiquinone undergoes aerobic oxidation [O] to generate  $O_2^{\bullet-}$  and the parent quinone. Under anaerobic conditions, the semiquinone could undergo a disproportionation reaction yielding quinone and the corresponding hydroquinone. Two-electron reduction ( $2e^-$ ) of quinone produces hydroquinone, which may undergo a compounding reaction with quinone to produce semiquinone that is oxidized to semiquinone and  $O_2^{\bullet-}$ , producing reactive alkylating agents and/or is excreted from the body. The semiquinones and  $O_2^{\bullet-}$  produced by the process eventually lead to oxidative stress and cell damage.

**Table S1.** HOMO, LUMO and IP energies calculated at the B3LYP/6-311++G\*\* level of theory, and scavenging activity on DPPH radical.

Comp.	Structure	$E_{\text{HOMO}}$ (eV)	$E_{\text{LUMO}}$ (eV)	$E_{\text{gap}}$ (eV)	IP(O <sup>a</sup> ) (eV)	IP(E <sup>b</sup> ) (eV)	Scavenging activity on DPPH <sup>c</sup> (μM)
Aloe-emodin (2)		-6.6	-3.11	3.48	6.6	0.29	222 [150]
Aloesone		-6.67	-1.06	5.07	6.67	0.30	351 [150]
Isoeleutheol		-5.97	-1.88	4.09	5.97	0.23	217 [151]

HOMO, highest occupied molecular orbital; LUMO, lowest unoccupied molecular orbital; IP, ionization potential; O<sup>a</sup>, orbital consideration (orbital-vertical); E<sup>b</sup>, energy consideration (energy-vertical); DPPH<sup>c</sup>, Trolox equivalents.

**Table S2.** The BDE value of free radical species (1-OH, 3-OH, and 8-OH) of emodin (1).

	Calculating method	BDE (kJ·mol <sup>-1</sup> )
1-OH	B3LYP/6311++ G**	412.25
3-OH	B3LYP/6311++ G**	371.12
8-OH	B3LYP/6311++ G**	408.57

BDE: bond dissociation enthalpy.

**Table S3.** ΔBDE, ΔPDE, and ΔIP values of OH groups in purpurin (10) (relative to phenol).

	ΔBDE (kJ/mol)			ΔPDE (kJ/mol)			ΔIP (kJ/mol)
	1-OH	2-OH	4-OH	1-OH	2-OH	4-OH	
$P_{\text{gas}}$	-16.85	-25.39	-47.81	84.51	102.61	29.66	-51.81
$P_{\text{pcm}}$	1.32	-10.67	-27.04	-223.08	-231.83	-198.48	-10.65

All theoretical values refer to phenol calculated with the same method.

BDE, bond dissociation enthalpy; PDE, proton dissociation enthalpy; IP, ionization potential; pcm, polarizable continuum solvation mode.

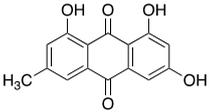
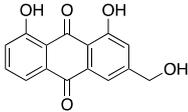
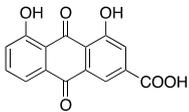
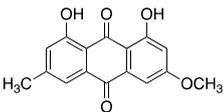
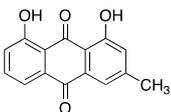
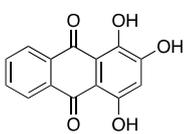
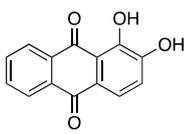
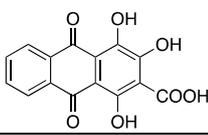
**Table S4.** The pharmacokinetic parameters of anthraquinones in dogs (Feng et al., 2014; Wang et al., 2021).

Comp.	$C_{\text{max}}$ (μg/ml)	$T_{\text{max}}$ (h)	AUC <sub>0-∞</sub> (mg h/l)
Emodin (1)	0.27–0.48	0.75–1.42	1.38–4.05
Aloe-emodin (2)	0.03–0.45	0.75–1.55	0.35–1.61
Rhein (3)	1.44–3.39	0.71–1.50	4.24–35.1

<b>Physcion (4)</b>	0.03	2.00	0.41
<b>Chrysophanol (5)</b>	0.03–0.30	1.00–2.00	0.43–0.83

$C_{max}$ , peak concentration;  $T_{max}$ , peak time; AUC, area under the curve.

**Table S5.** Radical scavenging activity of hydroxyanthraquinones (Cai et al., 2004).

Hydroxyanthraquinones	Structure	Equivalent antioxidant activity values
1		$0.172 \pm 0.002$ mM
2		$0.173 \pm 0.001$ mM
3		$0.174 \pm 0.001$ mM
4		$0.171 \pm 0.002$ mM
5		$0.170 \pm 0.001$ mM
10		$1.680 \pm 0.009$ mM
11		$1.019 \pm 0.008$ mM
12		$1.216 \pm 0.011$ mM