

Supplementary Material

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

Lihua Zhao¹ and Lin Zheng^{2,*}

¹ Tianjin Renai College, Tianjin 301636, China; huazi.95@163.com

² 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; H_2O_2 , hydrogen peroxide; 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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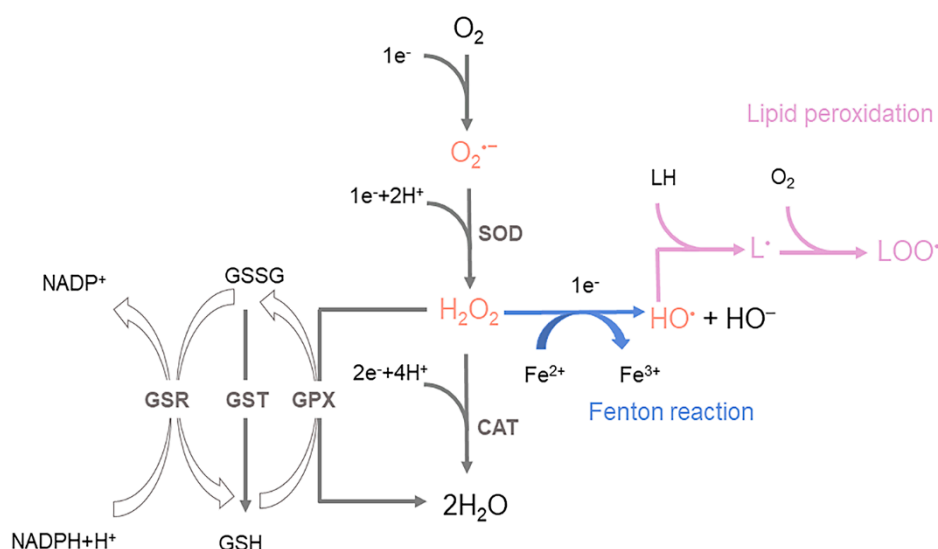


Figure S1. The illustration of ROS formation. The symbols and abbreviations are as follows: $\cdot OH$, hydroxyl radical; $O_2^{\cdot-}$, superoxide radical; H_2O_2 , hydrogen peroxide; OH^- , hydroxide anion; SOD, superoxide dismutase; CAT, catalase; GPX, glutathione peroxidase; GSH, reduced glutathione; GSSG, oxidized glutathione; GSR, glutathione reductase; GST, glutathione S-transferase.

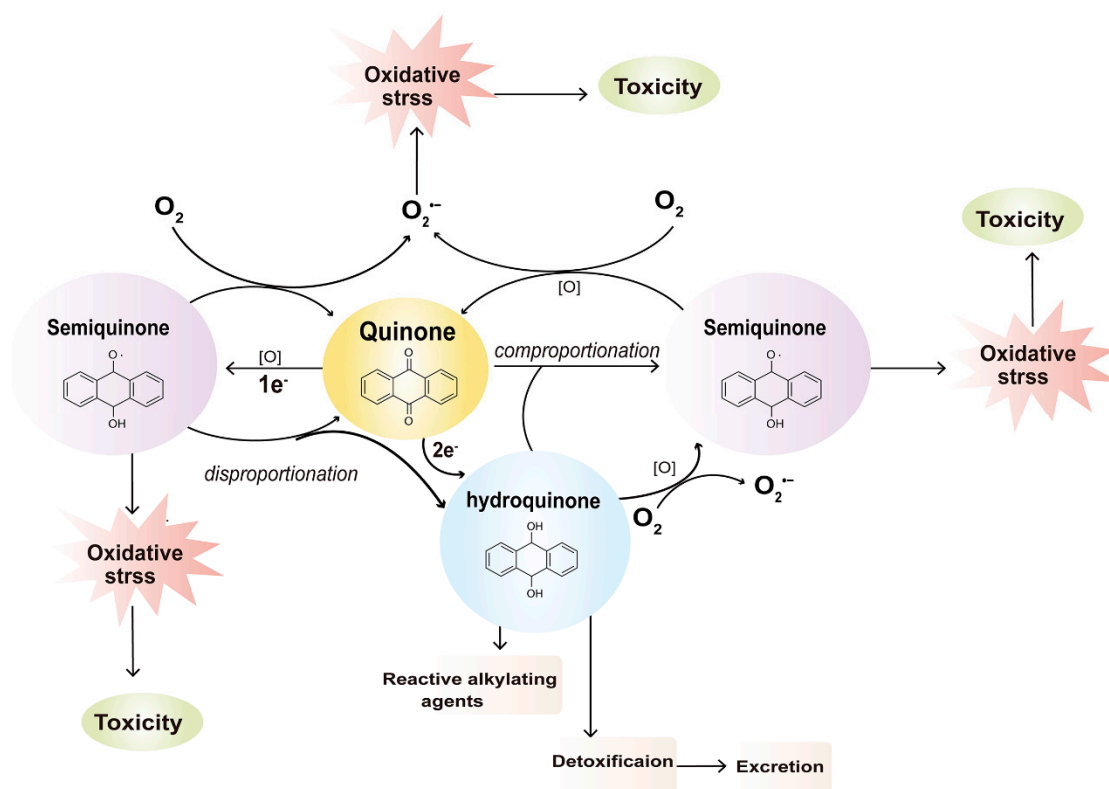
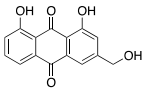
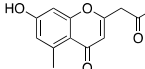
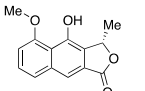


Figure S2. Redox cycling of quinones and the effect of the different components. One-electron reduction ($1e^-$) of the semiquinone undergoes aerobic oxidation [O] to generate $O_2^{\cdot-}$ and the parent quinone. Under anaerobic conditions, the semiquinone could undergo a disproportionation reaction 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 $O_2^{\cdot-}$, producing reactive alkylating agents and/or is excreted from the body. The semiquinones and $O_2^{\cdot-}$ 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_{HOMO} (eV)	E_{LUMO} (eV)	E_{gap} (eV)	IP(O ^a) (eV)	IP(E ^b) (eV)	Scavenging activity on DPPH ^c (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^a, orbital consideration (orbital-vertical); E^b, energy consideration (energy-vertical); DPPH^c, 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 ⁻¹)
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_{gas}	-16.85	-25.39	-47.81	84.51	102.61	29.66	-51.81
P_{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.

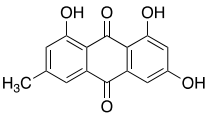
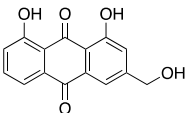
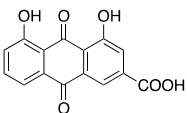
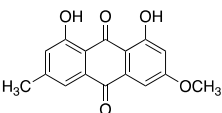
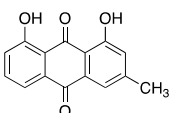
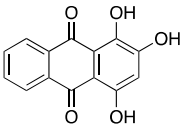
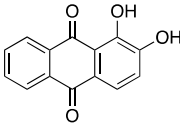
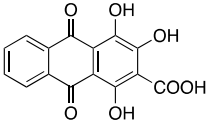
Table S4. The pharmacokinetic parameters of anthraquinones in dogs (Feng et al., 2014; Wang et al., 2021).

Comp.	C _{max} (μg/ml)	T _{max} (h)	AUC _{0-∞} (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

Physcion (4)	0.03	2.00	0.41
Chrysophanol (5)	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 ± 0.002 mM
2		0.173 ± 0.001 mM
3		0.174 ± 0.001 mM
4		0.171 ± 0.002 mM
5		0.170 ± 0.001 mM
10		1.680 ± 0.009 mM
11		1.019 ± 0.008 mM
12		1.216 ± 0.011 mM