

***Supporting Information for***

**Toxins in Botanical Dietary Supplements: Blue Cohosh Components Disrupt Cellular Respiration and Mitochondrial Membrane Potential**

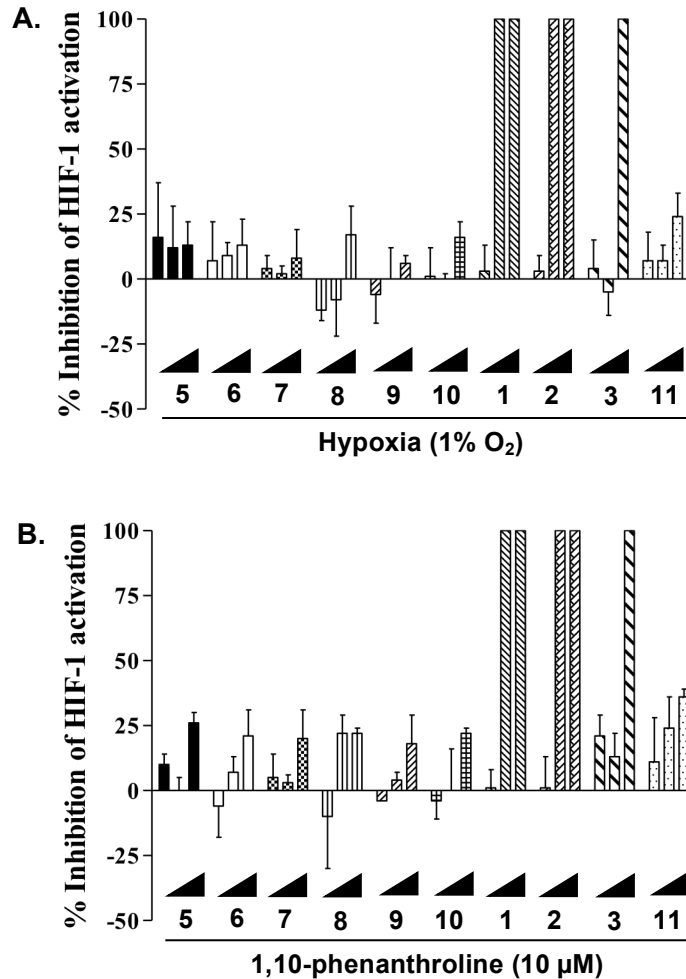
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**Figure S1. *C. thalictroides* compounds examined in the HIF assay.....S1**  
**Figure S2. Effects of blue cohosh compounds on HIF-1 activation. ....S2**  
**Figure S3. Effect of FCCP on cellular respiration.....S3**





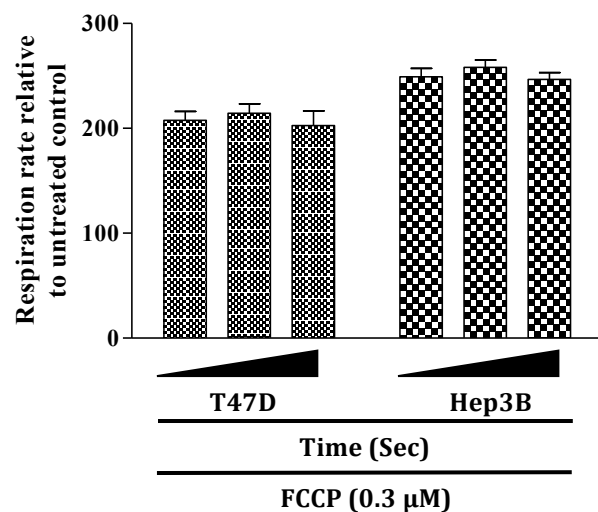
**Figure S2. Effects of blue cohosh pure compounds on HIF-1 activation.** A. Transfected (pTK-HRE3-luc) T47D cells were treated with compounds at incremental concentrations of 1, 10 and 30  $\mu\text{M}$  under hypoxic (1%  $\text{O}_2$ ) conditions for 16 h. Luciferase activities are presented as "% Inhibition" of the induced control. Data shown are average + SD from one representative experiment ( $n = 3$ ). B. Conditions similar to those described in A, except that HIF-1 was induced with 1,10-phenanthroline (10  $\mu\text{M}$ ).

Cycloheximide (protein synthesis inhibitor) and rotenone (mitochondrial respiration inhibitor) were used as positive controls.

Control results:

A. cycloheximide (100  $\mu\text{M}$ ) inhibited hypoxia-induced HIF-1 activation by 98% ( $\pm 0\%$  SD,  $n = 6$ ); rotenone (0.1  $\mu\text{M}$ ) inhibited HIF-1 activation by 89% ( $\pm 5\%$  SD,  $n = 6$ ).

B. cycloheximide (100  $\mu\text{M}$ ) inhibited 1,10-phenanthroline-induced HIF-1 activation by 98% ( $\pm 1\%$  SD,  $n = 3$ ); rotenone (0.1  $\mu\text{M}$ ) inhibited HIF-1 activation by 42% ( $\pm 6\%$  SD,  $n = 3$ ).



**Figure S3. Effect of FCCP on cellular respiration.** FCCP (0.3  $\mu\text{M}$ ) was added to intact T47D and Hep3B cells. Oxygen consumption rates were recorded 30, 115 and 295 s after compound addition and the data were normalized to that of the untreated control (Relative Respiration Rate:  $\text{Rate}_{\text{treated}}/\text{Rate}_{\text{control}} \times 100$ ). Positive values indicate a relative stimulation of oxygen consumption. Data shown are average + standard deviation from three independent experiments ( $n = 3$ ).