## Supplementary information to:

## *POLYGONUM MINUS* ESSENTIAL OIL MODULATES CISPLATIN-INDUCED HEPATOTOXICITY THROUGH INFLAMMATORY AND APOPTOTIC PATHWAYS

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Supplementary Figure 1: Flowchart of the effect of *P. minus* essential oil against cisplatin-induced hepatotoxicity



Supplementary Figure 2: MS chromatogram of P. minus essential oil

Supplementary Table	1: The mean and	SEM of the	effect of P.	minus essential	oil on CYP2E1
gene expression level	in the liver of cis	platin-induce	d hepatotox	icity rats	

Groups	Relative mRNA expression
	Mean ± SEM
Control (Normal Saline)	$1.00 \pm 0.10$
Cisplatin (10 mg/kg)	1.88 ± 0.24ª
BCP (150 mg/kg)	1.04 ± 0.11 <sup>b</sup>
PmEO100CP ( <i>P. minus</i> Essential Oil 100 mg/kg + Cisplatin 10 mg/kg)	1.14 ± 0.07 <sup>b</sup>
PmEO200CP ( <i>P. minus</i> Essential Oil 200 mg/kg + Cisplatin 10 mg/kg)	1.43 ± 0.10 <sup>b</sup>
PmEO400CP ( <i>P. minus</i> Essential Oil 400 mg/kg + Cisplatin 10 mg/kg)	$2.40 \pm 0.34^{\text{abcde}}$
PmEO400 ( <i>P. minus</i> Essential Oil 400 mg/kg)	1.74 ±0.06 <sup>acdf</sup>

Values are mean  $\pm$  SEM (n = 6).

<sup>a</sup>Significantly different from control group at p<0.05.

<sup>b</sup>Significantly different from cisplatin group p<0.05.

Significantly different from BCP group at p<0.05.

<sup>d</sup>Significantly different from PmEO100CP group at p<0.05.

<sup>°</sup>Significantly different from PmEO200CP group at p<0.05.

<sup>f</sup>Significantly different from PmEO400CP group at p<0.05.

Supplementary Table 2: The mean and SEM of the effect of *P. minus* essential oil on inflammation markers in the liver of cisplatin-induced hepatotoxicity rats

Crowno	TNF-α	IL-1α	IL-1β	IL-6	IL-10
Groups	Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM
Control (Normal Saline)	3.14 ± 0.30	138.01 ± 4.6	563.17 ± 35.35	3661.51 ± 208.30	912.31 ± 65.04
Cisplatin (10 mg/kg)	$7.20 \pm 0.37^{a}$	357.22 ± 10.91ª	915.30 ± 32.87 <sup>a</sup>	5030.50 ± 199.94 <sup>a</sup>	636.46 ± 18.20ª
BCP (150 mg/kg)	$4.47 \pm 0.54^{b}$	151.82 ± 6.93 <sup>b</sup>	676.74 ± 15.40 <sup>b</sup>	3854.20 ± 136.29 <sup>b</sup>	972.98 ± 59.44 <sup>b</sup>
PmEO100CP ( <i>P. minus</i> Essential Oil	4.01 ± 0.70 <sup>b</sup>	194.10 ± 24.83 <sup>b</sup>	591.46 ±74.60 <sup>b</sup>	3390.46 ± 408.90 <sup>b</sup>	878.60 ± 68.90 <sup>b</sup>
Too mg/kg + Cisplatin To mg/kg)					
200 mg/kg + Cisplatin 10 mg/kg)	$6.30 \pm 0.37^{a}$	$298.24 \pm 22.45^{acd}$	$865.25 \pm 60.06^{ad}$	6001.87 ± 197.33 <sup>acd</sup>	576.75 ± 54.76 <sup>acd</sup>
PmEO400CP ( <i>P. minus</i> Essential Oil 400 mg/kg + Cisplatin 10 mg/kg)	9.42 ± 1.08 <sup>acde</sup>	304.98 ± 26.91 <sup>acd</sup>	828.90 ± 56.13 <sup>ad</sup>	4849.26 ± 108.71 <sup>ade</sup>	$500.82 \pm 42.48^{\text{acd}}$
PmEO400 ( <i>P. minus</i> Essential Oil 400 mg/kg)	$3.35 \pm 0.48^{bef}$	191.96 ± 11.81 <sup>bef</sup>	553.41 ± 48.05 <sup>bef</sup>	3431.50 ± 291.75 <sup>bef</sup>	$504.68 \pm 34.27^{acd}$

Values are mean ± SEM (n=6).

<sup>a</sup>Significantly different from control group at p<0.05.

<sup>b</sup>Significantly different from cisplatin group at p<0.05.

<sup>°</sup>Significantly different from BCP group at p<0.05.

<sup>d</sup>Significantly different from PmEO100CP group at p<0.05.

<sup>e</sup>Significantly different from PmEO200CP group at p<0.05.

Significantly different from PmEO400CP group at p<0.05.

	Relative mRNA expression						
Groups	p53	Caspase 8	Bax	Apaf-1	Caspase 9	Caspase 3	Bcl-2
	Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM
Control (Normal Saline)	$1.00 \pm 0.02$	$1.00 \pm 0.00$	$1.00 \pm 0.00$	$1.00 \pm 0.00$	$1.00 \pm 0.00$	$1.00 \pm 0.00$	1.00 ± 0.10
Cisplatin (10 mg/kg)	$2.00 \pm 0.02^{a}$	2.51 ± 0.00ª	1.67 ±0.00ª	$2.80 \pm 0.00^{a}$	$4.94 \pm 0.00^{a}$	$6.26 \pm 0.06^{a}$	$0.25 \pm 0.00^{a}$
BCP (150 mg/kg)	0.64 ± 0.01 <sup>b</sup>	1.19 ± 0.01 <sup>b</sup>	$1.31 \pm 0.00^{b}$	1.31 ±0.00 <sup>b</sup>	1.11 ± 0.00 <sup>b</sup>	$2.98 \pm 0.09^{b}$	$0.89 \pm 0.00^{b}$
PmEO100CP ( <i>P. minus</i>							
Essential Oil 100 mg/kg +	0.59 ± 0.01 <sup>b</sup>	1.36 ± 0.00 <sup>b</sup>	$1.09 \pm 0.00^{b}$	1.32 ± 0.00 <sup>b</sup>	$1.22 \pm 0.00^{b}$	$2.50 \pm 0.05^{b}$	$0.85 \pm 0.00^{b}$
Cisplatin 10 mg/kg)							
PmEO200CP (P. minus							
Essential Oil 200 mg/kg +	$0.82 \pm 0.01^{b}$	1.84 ± 0.02	$1.86 \pm 0.00^{acd}$	2.00 ± 0.01	$2.27 \pm 0.00$	$5.25 \pm 0.04^{ad}$	$0.34 \pm 0.00^{a}$
Cisplatin 10 mg/kg)							
PmEO400CP ( <i>P. minus</i>							
Essential Oil 400 mg/kg +	$2.96 \pm 0.04^{\text{acde}}$	$2.42 \pm 0.02^{ac}$	1.87 ± 0.00 <sup>acd</sup>	$4.56 \pm 0.04^{\text{abcde}}$	$6.07 \pm 0.02^{acde}$	7.99 ± 0.07 <sup>acde</sup>	$0.05 \pm 0.00^{\text{acd}}$
Cisplatin 10 mg/kg)							
PmEO400 ( <i>P. minus</i>	$0.80 \pm 0.07$ bf	$1.60 \pm 0.01$	1 22 ± 0 00ef	2 55 ± 0 01bef	$0.06 \pm 0.00$ bf	1 01 ± 0 03bef	$0.30 \pm 0.003$
Essential Oil 400 mg/kg)	$0.00 \pm 0.07^{51}$	$1.00 \pm 0.01$	1.22 ± 0.00	2.00 ± 0.01001	0.90 ± 0.00 <sup>51</sup>	1.01 ± 0.03 <sup>ber</sup>	0.39 ± 0.00 <sup>a</sup>

Supplementary Table 3: The mean and SEM of the effect of *P. minus* essential oil on apoptosis gene expression in the liver of cisplatin-induced hepatotoxicity rats

Values are mean  $\pm$  SEM (n = 6).

<sup>a</sup>Significantly different from control group at p<0.05.

<sup>b</sup>Significantly different from cisplatin group at p<0.05.

<sup>°</sup>Significantly different from BCP group at p<0.05.

<sup>d</sup>Significantly different from PmEO100CP group at p<0.05.

<sup>e</sup>Significantly different from PmEO200CP group at p<0.05.

<sup>f</sup>Significantly different from PmEO400CP group at p<0.05.

Supplementary Table 4: The mean and SEM of the effect of P. minus essential oil on cytochrome
c protein expression in the liver of cisplatin-induced hepatotoxicity rats

<b>O</b> mmuna	Expression Level (Fold Change)		
Groups	Mean ± SEM		
Control (Normal Saline)	1.00 ± 0.05		
Cisplatin (10 mg/kg)	2.18 ± 0.01ª		
BCP (150 mg/kg)	$1.18 \pm 0.00^{b}$		
PmEO100CP ( <i>P. minus</i> Essential Oil 100 mg/kg + Cisplatin 10 mg/kg)	$0.95 \pm 0.02^{b}$		
PmEO200CP ( <i>P. minus</i> Essential Oil 200 mg/kg + Cisplatin 10 mg/kg)	$1.86 \pm 0.02^{ad}$		
PmEO400CP ( <i>P. minus</i> Essential Oil 400 mg/kg + Cisplatin 10 mg/kg)	2.31 ± 0.03 <sup>acd</sup>		
PmEO400 ( <i>P. minus</i> Essential Oil 400 mg/kg)	1.68 ± 0.05 <sup>ad</sup>		

<sup>a</sup>Significantly different from control group at p<0.05.

<sup>b</sup>Significantly different from cisplatin group at p<0.05.

°Significantly different from BCP group at p<0.05.

<sup>d</sup>Significantly different from PmEO100CP group at p<0.05.