

## Supplementary material

## Screening results in ER Binding, ERE-luciferase, and Alkaline Phosphatase Assays

Plant or sample name and plant part	Extract Type	<sup>1</sup> Binding		<sup>2,3</sup> ERE-luc		<sup>3,4</sup> ALP		<sup>3,4</sup> SRB		<sup>1</sup> Binding		<sup>2,3</sup> ERE-luc		
		ER alpha	ER beta	ER alpha	ER beta	Estrogenic	Antiestrogenic	Cytotoxicity	ER beta	ER beta	ER beta	ER beta		
17 $\beta$ estradiol	Control	<b>95 <math>\pm</math> 1</b>		<b>21 <math>\pm</math> 7</b>		<b>100 <math>\pm</math> 10</b>				<b>4 <math>\pm</math> 2</b>		<b>90 <math>\pm</math> 1</b>		<b>7 <math>\pm</math> 3</b>
4-hydroxy tamoxifen	Control	<b>96 <math>\pm</math> 1</b>		1 $\pm$ 0.1		0 $\pm$ 5		<b>94 <math>\pm</math> 1</b>		2 $\pm$ 1		<b>94 <math>\pm</math> 1</b>		1 $\pm$ 0.2
DMSO	Control	0		1 $\pm$ 0.2		1 $\pm$ 2		0 $\pm$ 5		1 $\pm$ 2		0		1 $\pm$ 0.2
<i>Alisma plantago-aquatica</i> (Water Plantain) rhizomes	Petroleum ether Dichloromethane 75% ethanol	31 $\pm$ 5 25 $\pm$ 13 2 $\pm$ 2		0.9 $\pm$ 0.4 2.4 $\pm$ 1.5 1.2 $\pm$ 0.4		-7.3 $\pm$ 4.2 -9.8 $\pm$ 11 -10.4 $\pm$ 7.8		-1.5 $\pm$ 13.3 3.3 $\pm$ 14 -2.1 $\pm$ 10.4		10.7 $\pm$ 16.2 -5.7 $\pm$ 7.8 -17.8 $\pm$ 11.8		<b>51 <math>\pm</math> 7</b> 26 $\pm$ 3 8 $\pm$ 6		2.3 $\pm$ 1.9 2.1 $\pm$ 1.3 0.8 $\pm$ 0.4
<i>Angelica sinensis</i> (Dang-Gui) roots	<sup>5</sup> Methanol <sup>5</sup> Petroleum ether <sup>5</sup> Chloroform <sup>5</sup> Butanol <sup>5</sup> Water	8 $\pm$ 7 <b>81 <math>\pm</math> 10</b> 19 $\pm$ 9 4 $\pm$ 3 7 $\pm$ 11		1.8 $\pm$ 0.5 <b>9.7 <math>\pm</math> 3.5</b> <b>5.9 <math>\pm</math> 3</b> <b>9.5 <math>\pm</math> 2.2</b> 1.3 $\pm$ 0.8		-2.3 $\pm$ 5.5 -4.7 $\pm$ 6.2 12.3 $\pm$ 4.7 12.4 $\pm$ 8.2 -0.3 $\pm$ 1.2		15.3 $\pm$ 8.8 <b>48.7 <math>\pm</math> 9.5</b> 19.4 $\pm$ 9.8 -16.3 $\pm$ 4.5 -13.5 $\pm$ 2.5		3.1 $\pm$ 17.1 16.4 $\pm$ 13.6 30.6 $\pm$ 8 3.3 $\pm$ 15.2 -9.4 $\pm$ 6.1		34 $\pm$ 5 <b>99 <math>\pm</math> 9</b> <b>46 <math>\pm</math> 6</b> 0 $\pm$ 2 0 $\pm$ 4		1.3 $\pm$ 0.6 1.1 $\pm$ 0.4 0.8 $\pm$ 0.5 1.2 $\pm$ 0.2 1 $\pm$ 0.1
<i>Asclepias tuberosa</i> (Butterfly weed) roots	Petroleum ether Dichloromethane 75% ethanol	<b>69 <math>\pm</math> 7</b> 16 $\pm$ 9 0 $\pm$ 2		1.1 $\pm$ 0.4 4.1 $\pm$ 3.1 3.9 $\pm$ 4.3		-17.9 $\pm$ 15.5 -26.5 $\pm$ 4.5 -10.3 $\pm$ 8.9		-9.1 $\pm$ 21 114.6 $\pm$ 6.7 110.1 $\pm$ 8.5		-19.9 $\pm$ 9.8 <b>106.1 <math>\pm</math> 5.3</b> <b>99.1 <math>\pm</math> 3.6</b>		<b>85 <math>\pm</math> 5</b> 32 $\pm$ 10 5 $\pm$ 8		1.1 $\pm$ 0.8 <b>10.7 <math>\pm</math> 0.8</b> 1.3 $\pm$ 1.1
<i>Beta vulgaris</i> (Beets) roots	Petroleum ether Dichloromethane 75% ethanol	35 $\pm$ 10 33 $\pm$ 11 6 $\pm$ 5		<b>4.7 <math>\pm</math> 1.9</b> 3.2 $\pm$ 2 1 $\pm$ 0.2		-2.4 $\pm$ 17.4 -2.3 $\pm$ 5.5 -7.4 $\pm$ 10.4		4.4 $\pm$ 14.8 <b>43.7 <math>\pm</math> 8.6</b> -8.7 $\pm$ 17.7		-15.9 $\pm$ 29.4 -20.2 $\pm$ 30.9 -14 $\pm$ 33.7		<b>44 <math>\pm</math> 7</b> 30 $\pm$ 5 8 $\pm$ 13		1.1 $\pm$ 0.3 1.1 $\pm$ 0.1 1.1 $\pm$ 0.4
<i>Cimicifuga americana</i> (Yellow cohosh) roots	Petroleum ether Dichloromethane 75% ethanol	37 $\pm$ 8 31 $\pm$ 5 9 $\pm$ 8		1.6 $\pm$ 0.7 2.8 $\pm$ 1.1 1.1 $\pm$ 0.2		-5.8 $\pm$ 14.4 -16.2 $\pm$ 14.9 -4.4 $\pm$ 14.3		27.1 $\pm$ 27.5 <b>79.2 <math>\pm</math> 19.5</b> -10 $\pm$ 12.4		-3.7 $\pm$ 37 5.8 $\pm$ 32.1 -22.4 $\pm$ 25		<b>47 <math>\pm</math> 10</b> 21 $\pm$ 9 7 $\pm$ 6		1.4 $\pm$ 0.3 1.4 $\pm$ 0.6 1 $\pm$ 0.1

<sup>1</sup> Percent binding at 200  $\mu$ g/mL.

<sup>2</sup> Fold Induction where DMSO is 1.

<sup>3</sup> Tested at 20  $\mu$ g/mL.

<sup>4</sup> Percent induction (estrogenic), inhibition (antiestrogenic), or cytotoxic.

<sup>5</sup> Fraction instead of partition.

<sup>6</sup> Bold face-type indicates assay activity.

Plant or sample name and plant part	Extract Type	<sup>1</sup> Binding		<sup>2,3</sup> ERE-luc		<sup>3,4</sup> ALP		<sup>3,4</sup> SRB		<sup>1</sup> Binding		<sup>2,3</sup> ERE-luc	
		ER alpha	ER beta	ER alpha	ER beta	Estrogenic	Antiestrogenic	Cytotoxicity	Cytotoxicity	ER beta	ER beta	ER beta	ER beta
<i>Cimicifuga racemosa</i> (Black cohosh) aerial parts	DCM extract	34 ± 7	<b>6.6 ± 3.2</b>	-2.5 ± 1.3	3.5 ± 8.7	8.3 ± 5.2		8.3 ± 5.2	45 ± 3	1.1 ± 0.4			
	75% EtOH	21 ± 5	<b>5.8 ± 1.8</b>	4.3 ± 5.3	<b>-48.4 ± 4.9</b>	0.1 ± 5.7		0.1 ± 5.7	23 ± 3	1 ± 0.2			
	PE extract	<b>55 ± 8</b>	3.2 ± 1.5	-4.5 ± 4.8	21.3 ± 7.2	4.8 ± 10.9		4.8 ± 10.9	<b>64 ± 8</b>	1 ± 0.5			
<i>Cimicifuga rubrifolia</i> (Appalachian bugbane) aerial parts	Petroleum ether	<b>56 ± 2</b>	2.5 ± 2	-13.1 ± 12.4	33.2 ± 17	-23.2 ± 25		-23.2 ± 25	<b>66 ± 6</b>	1.1 ± 0.5			
	Dichloromethane	<b>51 ± 5</b>	<b>7.4 ± 1.1</b>	0.3 ± 15.9	21 ± 14.2	4.4 ± 19.8		4.4 ± 19.8	40 ± 8	0.8 ± 0.3			
	75% ethanol	4 ± 3	2.3 ± 1.4	6 ± 13	-30.5 ± 22.1	6.8 ± 11.7		6.8 ± 11.7	4 ± 7	1.1 ± 0.6			
<i>Cornus officinalis</i> (Dogwood) fruits	Petroleum ether	26 ± 16	<b>24.3 ± 6.6</b>	2.6 ± 5.9	41.8 ± 4.1	11.5 ± 3.4		11.5 ± 3.4	<b>48 ± 4</b>	1.5 ± 0.5			
	Dichloromethane	0 ± 4	2.5 ± 0.7	-2.2 ± 4.8	24.9 ± 5.2	<b>30.6 ± 19.1</b>		<b>30.6 ± 19.1</b>	0 ± 2	1.3 ± 0.3			
	75% ethanol	17 ± 2	0.5 ± 0.7	-0.2 ± 7.9	-10.8 ± 6.3	-8.9 ± 6.1		-8.9 ± 6.1	5 ± 3	1 ± 0.5			
<i>Daucus carota</i> (Carrots) roots	Petroleum ether	21 ± 6	<b>12.3 ± 5.1</b>	-6.8 ± 11.2	-26.6 ± 14.6	-18.7 ± 19.1		-18.7 ± 19.1	36 ± 6	0.9 ± 0.5			
	Dichloromethane	22 ± 5	<b>5.4 ± 1.8</b>	-5.7 ± 8	-11.5 ± 16.1	13.7 ± 14.1		13.7 ± 14.1	26 ± 6	0.7 ± 0.2			
	75% ethanol	8 ± 8	0.8 ± 0.6	-7.7 ± 8.7	-19.5 ± 14.9	-6.3 ± 9.5		-6.3 ± 9.5	19 ± 10	1 ± 0.5			
<i>Paeonia moutan</i> (Peony) bark	Petroleum ether	21 ± 5	2.8 ± 1	-9.7 ± 11.4	8.7 ± 16.7	7.7 ± 19.7		7.7 ± 19.7	<b>60 ± 6</b>	2 ± 1.7			
	Dichloromethane	19 ± 6	3.4 ± 2.8	-10.7 ± 13	24.4 ± 14.7	11.5 ± 16.1		11.5 ± 16.1	19 ± 5	1.8 ± 0.2			
	75% ethanol	14 ± 13	0.8 ± 0.3	-10 ± 8.9	-30.2 ± 22.7	-10.1 ± 18.3		-10.1 ± 18.3	3 ± 5	1 ± 0.4			
<sup>7</sup> <i>Polygonum multiflorum</i> (Fo-Ti) roots	Petroleum ether	15 ± 8	<b>21.7 ± 8.5</b>	6.5 ± 1.8	1.2 ± 3.3	7.6 ± 14.3		7.6 ± 14.3	<b>50 ± 9</b>	1.4 ± 0.7			
	Dichloromethane	30 ± 7	<b>25.8 ± 11.2</b>	12.3 ± 3.4	0.4 ± 12.3	12.7 ± 17.8		12.7 ± 17.8	36 ± 13	3 ± 2.5			
	75% ethanol	4 ± 3	1.5 ± 0.2	0.7 ± 3.3	3.9 ± 18.2	2.7 ± 7.5		2.7 ± 7.5	0 ± 3	1.2 ± 1.1			
<sup>8</sup> <i>Polygonum multiflorum</i> (Fo-Ti) roots	Petroleum ether	22 ± 16	<b>15.1 ± 9.1</b>	-1.5 ± 0.6	36.1 ± 48.6	18.4 ± 22.6		18.4 ± 22.6	26 ± 9	1.2 ± 0.9			
	Dichloromethane	16 ± 5	<b>16 ± 3.4</b>	-0.2 ± 1.6	68.3 ± 11.5	<b>31.1 ± 19.1</b>		<b>31.1 ± 19.1</b>	16 ± 7	0.9 ± 0.7			
	75% ethanol	5 ± 3	0.7 ± 0.2	-0.4 ± 2.5	16.5 ± 26.2	18 ± 20.5		18 ± 20.5	0 ± 3	1 ± 0.2			
<i>Pueraria lobata</i> (Kudzu) aerial parts	Petroleum ether	32 ± 2	<b>10.3 ± 2.8</b>	-10.8 ± 12.6	<b>46.9 ± 18.9</b>	12.7 ± 30		12.7 ± 30	36 ± 2	1.5 ± 1.4			
	Dichloromethane	<b>63 ± 6</b>	<b>24.5 ± 9.9</b>	-0.3 ± 25.6	36 ± 32.6	-3.3 ± 5.5		-3.3 ± 5.5	<b>45 ± 19</b>	1.2 ± 0.5			
	75% ethanol	17 ± 16	<b>26.9 ± 12.7</b>	-1.3 ± 13.8	28.9 ± 40.7	7.6 ± 50.1		7.6 ± 50.1	<b>63 ± 3</b>	<b>3.5 ± 1.3</b>			
<i>Pueraria mirifica</i> (Kwao Keur) bark	Petroleum ether	12 ± 8	<sup>9</sup> N.T.	-2.7 ± 2.6	58.5 ± 37	<b>100.6 ± 38.8</b>		<b>100.6 ± 38.8</b>	18 ± 12	N.T.			
	Dichloromethane	12 ± 5	<b>25.7 ± 9.5</b>	-4.2 ± 1.1	101.1 ± 8.6	<b>115 ± 2.2</b>		<b>115 ± 2.2</b>	19 ± 11	3.2 ± 1.6			
	75% ethanol	18 ± 7	<b>28 ± 8.6</b>	-1.4 ± 4.8	52.2 ± 61	<b>60.4 ± 62.2</b>		<b>60.4 ± 62.2</b>	31 ± 8	2.4 ± 1.3			
<i>Valeriana officinalis</i> (Valerian)	Petroleum ether	<b>43 ± 11</b>	<b>7.2 ± 3.1</b>	-7.8 ± 7.6	33.7 ± 16.8	12.5 ± 19.3		12.5 ± 19.3	<b>81 ± 4</b>	1.3 ± 0.8			
	Dichloromethane	13 ± 12	<b>5.9 ± 1.6</b>	-8.5 ± 7.7	19.4 ± 8.2	-7.6 ± 21		-7.6 ± 21	13 ± 6	0.7 ± 0.1			

<sup>7</sup> BC number 268.

<sup>8</sup> BC number 286.

<sup>9</sup> Not tested due to the limited quantities available.

Plant or sample name and plant part	Extract Type	<sup>1</sup> Binding		<sup>2,3</sup> ERE-luc		<sup>3,4</sup> ALP		<sup>3,4</sup> SRB		<sup>1</sup> Binding		<sup>2,3</sup> ERE-luc	
		ER alpha	ER alpha	ER alpha	Estrogenic	Antiestrogenic	Cytotoxicity	ER beta	ER beta	ER beta	ER beta		
roots	75% ethanol	12 ± 6	1.7 ± 1.1	-10.4 ± 9.5	-0.8 ± 5.4	-18.9 ± 15.6	7 ± 11	7 ± 11	1.1 ± 0.5				
<i>Viburnum opulus</i> (Guelder Rose)	Petroleum ether	17 ± 17	1.3 ± 0.4	-0.3 ± 0.9	-2.1 ± 5.8	7.1 ± 12.6	11 ± 8	11 ± 8	1.2 ± 0.6				
bark	Dichloromethane	11 ± 4	1.4 ± 0.2	1.6 ± 1.4	14 ± 7.4	22.5 ± 4	6 ± 2	6 ± 2	0.8 ± 0.2				
	75% ethanol	22 ± 10	1.4 ± 0.3	-1.2 ± 0.7	-17.5 ± 11.4	11.4 ± 6.9	24 ± 16	24 ± 16	0.7 ± 0.6				
<i>Viburnum prunifolium</i> (Black Haw)	Petroleum ether	12 ± 6	0.8 ± 0.3	-3.7 ± 0.7	-9.8 ± 0.8	7.7 ± 5.7	6 ± 3	6 ± 3	1 ± 0.5				
bark	Dichloromethane	3 ± 6	0.7 ± 0.5	-3.5 ± 3	68.5 ± 6.3	<b>42 ± 4.4</b>	3 ± 4	3 ± 4	1 ± 0				
	75% ethanol	10 ± 10	4.9 ± 3.7	-0.5 ± 2.2	-33 ± 7.9	-2.7 ± 11.2	3 ± 9	3 ± 9	0.9 ± 0.6				
<i>Vitex agnus-castus</i> (Chasteberry)	Petroleum ether	37 ± 6	<b>9.5 ± 2.5</b>	-1.1 ± 1.6	43.5 ± 3.3	<b>39.1 ± 8.3</b>	<b>68 ± 9</b>	<b>68 ± 9</b>	1.1 ± 0.7				
fruits	Dichloromethane	13 ± 3	<b>9.6 ± 6.6</b>	-2.3 ± 1.5	94.5 ± 7.2	<b>112.5 ± 8.8</b>	20 ± 19	20 ± 19	0.8 ± 0.3				
	75% ethanol	10 ± 8	2.3 ± 0.9	-1.5 ± 2.7	-14.3 ± 7.6	2.3 ± 7.9	7 ± 7	7 ± 7	1.3 ± 0.7				