1   **Supplementary Material**

2   Preparation of DCQD, XCQD, HPDHD, HPSWD and three single-herb decoctions

3   The DCQD was prepared according to the method and procedure described in Shang-Han-Lun and was

4   optimized [11]: the bark of *Magnolia officinalis Rehd* (Magnoliaceae, 24 g) and *Fructus Aurantii Immaturus*

5   (Rutaceae, 15 g) were immersed in 200 mL distilled water for 30 min and boiled until half of the original amount

6   was left. This procedure was repeated. The two water extracts were combined. the root and bark of *Radix et*

7   *Rhizoma Rhei* (Polygonaceae, 12 g) were then immersed in the above mentioned combined water extracts for

8   20min and boiled until half of the original amount was left and this procedure was repeated in 200 mL distilled

9   water. The two water extracts were combined and then *Mirabilitum* (mirabilite, crystals of sodium sulfate, Na_2SO_4,

10 6 g) was dissolved in the water extract. The extract was then filtered and diluted to 250mL with distilled water and

11 stored at -80 ◦C until use.

12 The XCQD was prepared as follows: the root and bark of *Radix et Rhizoma Rhei* (12 g), the bark of *Magnolia*

13 *officinalis Rehd* (6 g) and *Fructus Aurantii Immaturus* (9 g) were immersed in 300mL distilled water for 30min

14 and boiled until half of the original amount was left. This procedure was repeated in 200 mL distilled water. The

15 two water extracts were combined and diluted to 250 mL with distilled water and stored at -80 ◦C until use.

16 The HPDHD was prepared just as XCQD: the root and bark of *Radix et Rhizoma Rhei* (18 g), the bark of

17 *Magnolia officinalis Rehd* (24 g) and *Fructus Aurantii Immaturus* (12 g) were immersed in 300mL distilled water

18 for 30 min and boiled until half of the original amount was left. This procedure was repeated in 200 mL distilled

19 water. The two water extracts were combined and diluted to 250mL with distilled water and stored at -80 ◦C until

20 use.

21 The HPSWD was prepared just as DCQD without adding *Mirabilitum*.

22 Single-herb decoctions of the root and bark of *Radix et Rhizoma Rhei* (12g), the bark of *Magnolia officinalis*

23 *Rehd* (24g), *Fructus Aurantii Immaturus* (15g) were immersed in 200mL distilled water for 30min respectively and

24 boiled until half of the original amount was left. This procedure was repeated in 200 mL distilled water. The two

25 water extracts were combined and diluted to 250mL with distilled water and stored at -80 ◦C until use.

26

27

28

29

30

31

Table 1 The features generated after each filtering step

|	Total Features generated using Profiling Solution	features left after 80% rule		features left after VIP >1	
		positive	negative	positive	negative
Mangnolia officinalis	717	65	110	19	26
Radix et Rhizoma Rhei	714	54	122	16	24
fructus Aurantii Immaturus	713	138	244	34	48

32

33

34

Table 2 Components identified from DCQD, XCQD, HPDHD, HPSWD in detail

Peak no.	t_R(min)	Assigned identity	VIP	P value	polarity	origin
1	1.267	citric acid	1.50922	0.005	–	
2	5.582	catechin	1.40609	0.044	+	*Radix et Rhizoma Rhei*
3	10.117	Cinnamoyl glucose1	1.08846	0.034	+	
4	12.033	Cinnamoyl glucose2	1.04518	0.002	+	
5	23.757	rhein	1.40394	0.016	–	
6	10.535	Magloside A	1.37919	0.003	–	
7	14.348	magnolol B	1.12307	0.016	–	
8	14.592	Acteoside	1.01294	0.002	–	
9	14.906	Magloside E	2.64475	0.004	–	*Mangnolia officinalis*
10	18.603	magnolignan A	1.34576	0.02	–	
11	21.456	Magnaldehyde D	1.10664	0.005	–	
12	22.689	Magnaldehyde B	1.33	0.044	–	
13	24.633	magnolol	2.91069	0.001	–	
14	0.915	Scopoletin	1.92575	0.015	–	
15	1.018	synephrine	1.17819	0.006	+	
16	1.216	3,5-dihydroxy phenyl 1-O-β-D-glycosidase	1.78352	0.01	–	
17	1.553	adenosine	1.12193	0.014	+	
18	12.393	Neoeriocitrin	1.61417	0.008	–	
19	13.964	naringin	2.43343	0.042	–	*fructus Aurantii Immaturus*
20	14.596	Hesperitin-glucoside	1.02867	0.036	–	
21	14.781	hesperidin	1.20988	0.002	+	
22	14.947	neohesperidin	2.23212	0.002	–	
23	15.445	Rhoifolin	1.03341	0.008	–	
24	18.064	limonin	1.15561	0.023	+	
25	21.398	Marmin	1.60869	0.004	+	
26	24.063	tangeretin	1.39182	0.005	+	

35

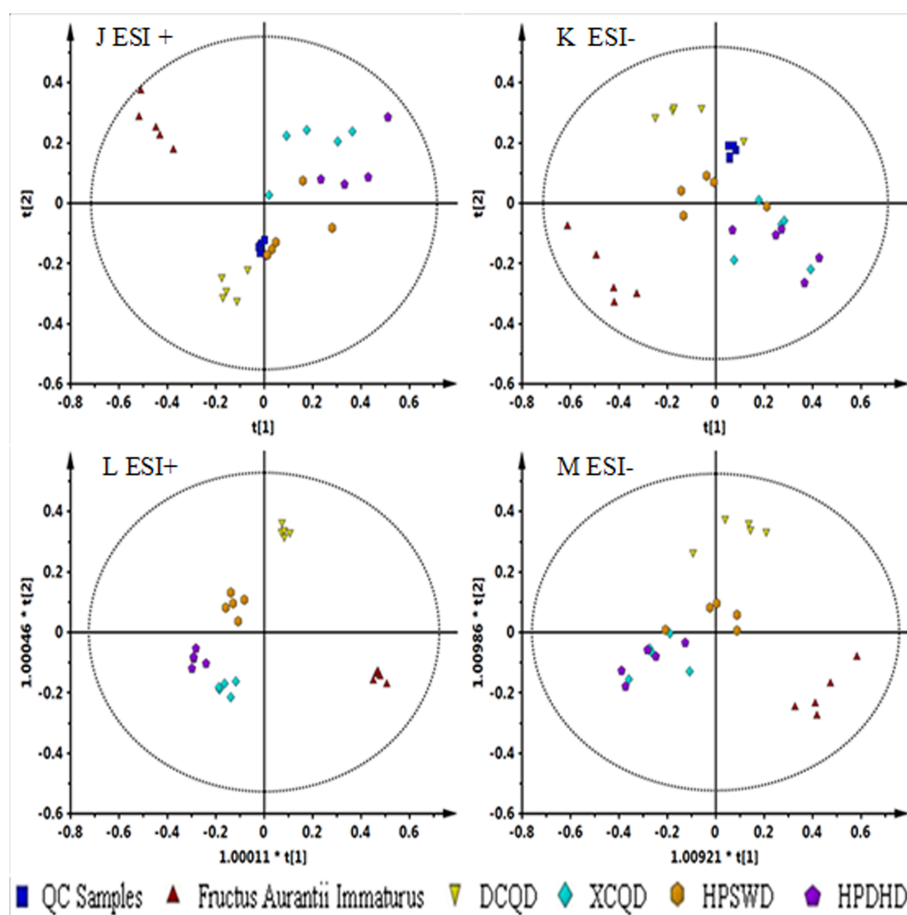36
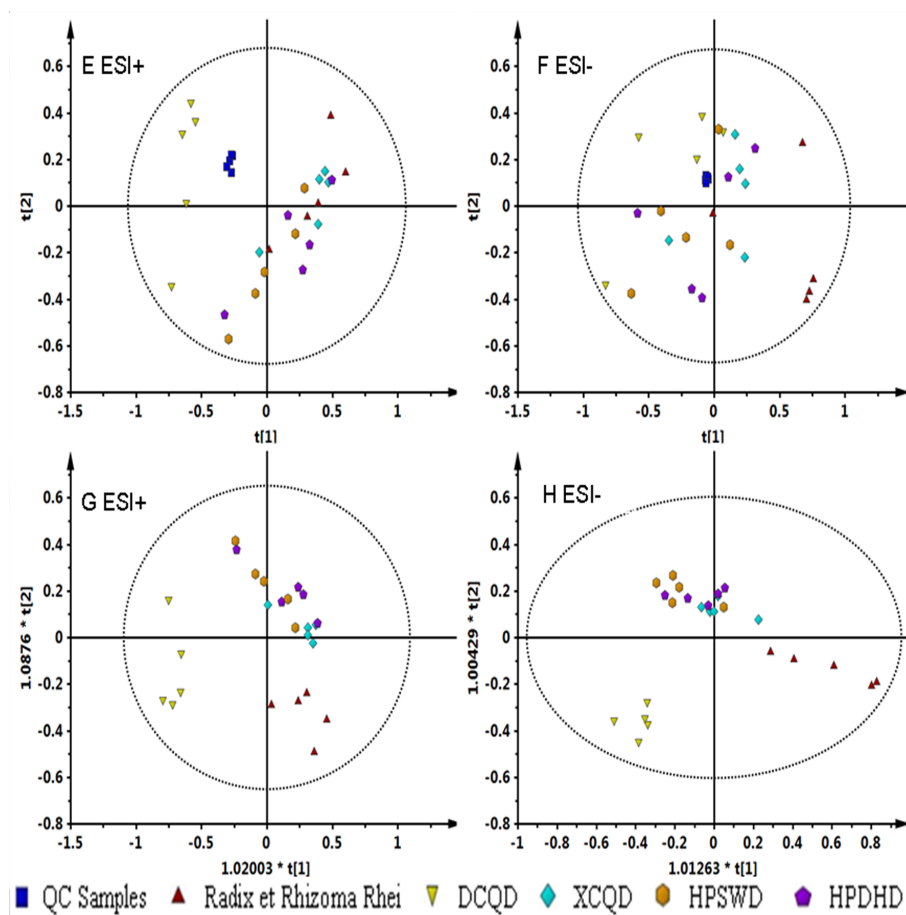
Fig.A Scores plots of principal components analysis (PCA) (E: ESI+; F: ESI-) and orthogonal partial least squares

discriminant analysis (OPLS-DA) (G: ESI+; H: ESI-) models of the peaks of *Radix et Rhizoma Rhei* with the

statistical parameters as follows: E $R^2X=0.811$, $Q^2=0.315$; F $R^2X=0.648$, $Q^2=0.463$; G $R^2X=0.665$, $R^2Y=0.688$,

$Q^2=0.323$; H $R^2X=0.617$, $R^2Y=0.458$, $Q^2=0.327$.

41

Fig.B Scores plots of principal components analysis (PCA) (J: ESI+; K: ESI-) and orthogonal partial least squares

discriminant analysis (OPLS-DA) (L: ESI+; M: ESI-) models of the peaks of *Fructus Aurantii Immaturus* with the

statistical parameters as follows: J $R^2X=0.701$, $Q^2=0.294$; K $R^2X=0.648$, $Q^2=0.463$; L $R^2X=0.854$, $R^2Y=0.981$,

$Q^2=0.709$; M $R^2X=0.586$, $R^2Y=0.845$, $Q^2=0.342$.