

Supporting Information

**TEXT 1S MEDICAL QUESTIONNAIRE**

Full Name		Occupation	
<b>Address</b>			
<b>E-mail Address</b>			
<b>Weight</b>		<b>Height</b>	
<b>Marital Status</b>		<b>Fertility Status</b>	

**Statement of Health**

*The Medical Examiner is requested to ask the following questions or to review them if they have been answered previously. Give details and dated if any of the questions below are answered with "Yes"*

1. Do you currently have any health problems? Yes  No

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2. Have you ever been hospitalized? Yes  No

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3. Have you visited a doctor in the last three (3) years? Yes  No

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4. Do you suffer from or have you ever suffered from any of the following

(a) Tuberculosis Yes  No

(b) Leprosy Yes  No

(c) Hepatitis (specify type) Yes  No

(d) Typhoid, dysentery or any other infectious or Communicable diseases Yes  No

(e) AIDS or AIDS related conditions, any Immune Deficiency Syndrome Yes  No

(f) Genetic or Familial Disorders Yes  No

(g) Deafness or Chronic Ear Disease Yes  No

(h) Blindness or Eye Disease Yes  No

(i) Any cancerous disease: benign/malignant Yes  No

(j) Headache migraine, epilepsy or dizziness Yes  No

(k) Nervous or mental illness or disorders Yes  No

(l) Any allergies, asthma or pulmonary disease Yes  No

(m) Cardiovascular diseases, arterial Hypertension Yes  No

(n) Liver, stomach or intestinal diseases Yes  No

(o) Diabetes or other hormone diseases Yes  No

(p) Urinary tract disease Yes  No   
(q) Venereal diseases Yes  No   
(r) Rheumatism, Muscle, Joint or bone diseases Yes  No   
(s) Skin diseases Yes  No   
(t) Cosmetic operations Yes  No   
(u) Any other illness or disorder Yes  No

If "Yes" to any of the above, please give details and dates.

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## 5. How old do you first menarche?

## 6. How long of your menstrual cycle?

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Page 10 of 10

## 7. What about your menstrual quality?

- Color red, without blood clot    Color bleed, no congestion    Color bleed, with blood clot
- Color red, with blood clot

8. Do you have any dysmenorrheal history?

Yes  No

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9. When do you feel pain in menstrual period?

Before menstruation  During menstruation  After menstruation

10. What's duration of your dysmenorrheal?

1 Day  2 Days  3 Days   $\geq 4$  Days

11. How long do you suffer dysmenorrheal?

1 Year  2-3 Years  4-5 Years   $\geq 6$  Years

12. What type of dysmenorrhea do you think you suffered?

Primary dysmenorrhea    Secondary dysmenorrhea    Uncertain

13. What do you think the reason caused dysmenorrhea?

- High pressure    Nervous in menstruation    Not pay attention to diet and keep warm in menstruation    Genetic factors    Irregular sleep    Environmental factors

14. How symptoms accompany with your dysmenorrhea?

Abdominal pain, distension, lumbago    Nausea, vomiting and diarrhea     
Anxiety    Breast distending pain    Weak    Headache or dizziness

15. What dysmenorrheal degree do you think you suffered?

Mild: Not to affect the life    Moderate: Affect the life    Severe: Affect the life severely

16. How do you deal with dysmenorrhea?

Not to do anything, just rest    Visit a doctor    Take tradition Chinese medicine  
 Take analgesics    Do some exercises

*The Medical Examiner is required to examine the applicant and to answer the following questions. Give details and dates if any of the questions below are answered with "Yes".*

17. **Gynecological examination**-Any signs of abnormalities?      Yes    No

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18. **B-ultrasound examination**-Any signs of abnormalities?      Yes    No

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19. **Symptoms in traditional Chinese medicine**-Any signs of Qi stagnation syndrome?      Yes    No

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**20. Comments**

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**Important: Please attach original results of the following**

**(i) Routine Blood and urine test**

**(ii) B-ultrasound test**

**Medical Examiner's Details and Declaration**

<b>Full Name and Qualifications</b>			
<b>Specialty</b>		<b>Address</b>	
<b>Email Address</b>			<b>Telephone</b>

**I hereby confirm that I have identified, questioned and examined the applicant and have answered all questions to the best of my knowledge and in good faith.**

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Signature of Medical Examiner

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Place and Date of Examination

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Name and Stamp of Medical Examiner

**Table 1S.** Clinical Efficacy Assessment standard of Primary Dysmenorrhea

Symptoms	Scores
Abdominal pain during the menstrual cycle or before and after menstruation	Yes 5; No 0
Obviously abdominal pain	Yes 5.5; No 0
Abdominal pain is unbearable	Yes 6; No 0
Abdominal pain is unable to sit down or sleep at ease	Yes 1; No 0
Abdominal pain effects of work and study	Yes 1; No 0
Abdominal pain and need bed rest	Yes 1; No 0
Using the general measures and relief the pain	Yes 0.5; No 0
Using the general measures and afford no relief the pain	Yes 1; No 0
Pale	Yes 0.5; No 0
Cold sweat	Yes 1; No 0
Peripheral coldness	Yes 1; No 0
Schock	Yes 2; No 0
With the waist ache	Yes 0.5; No 0
With the nausea and vomiting	Yes 0.5; No 0
With anal bulge	Yes 0.5; No 0
Pain duration add one day the score add 0.5	Yes days $\times$ 0.5; No 0

**Table 2S.** UPLC - MS analytic results of Xiang-Fu-Si-Wu Formula

No.	t <sub>R</sub> min	Ion mode	Measured Mass( <i>m/z</i> )	Calc. Mass( <i>m/z</i> )	Error (ppm)	Elemental composition	Compound	Quantit ative ions	Content (mg/g dry extract)
1	1.86	neg	169.0136	169.0137	-0.1	C <sub>7</sub> H <sub>5</sub> O <sub>5</sub> <sup>-</sup>	Gallic acid <sup>a</sup>	169.0	6.68
2	8.79	neg	179.0318	179.0344	-1.5	C <sub>9</sub> H <sub>7</sub> O <sub>4</sub> <sup>-</sup>	Caffeic acid <sup>a</sup>	179.0	1.72
3	9.72	neg	353.0812	353.0873	-1.7	C <sub>16</sub> H <sub>17</sub> O <sub>9</sub> <sup>-</sup>	Chlorogenic acid <sup>a</sup>	353.1	8.13
4	12.77	neg	479.1437	479.1553	-2.4	C <sub>23</sub> H <sub>27</sub> O <sub>11</sub> <sup>-</sup>	Albiflorin <sup>a</sup>	479.1	54.4
5	13.45	neg	479.1416	479.1553	-2.9	C <sub>23</sub> H <sub>27</sub> O <sub>11</sub> <sup>-</sup>	Peoniflorin <sup>a</sup>	479.1	68.7
6	16.11	neg	193.0488	193.0501	-0.7	C <sub>10</sub> H <sub>9</sub> O <sub>4</sub> <sup>-</sup>	Ferulaic acid <sup>a</sup>	193.0	6.91
7	23.78	neg	249.1477	249.1491	-0.6	C <sub>15</sub> H <sub>21</sub> O <sub>3</sub> <sup>-</sup>	Neolazppaic acid	249.1	3.22 <sup>b</sup>
8	30.01	neg	203.0679	203.0708	-1.4	C <sub>12</sub> H <sub>11</sub> O <sub>3</sub> <sup>-</sup>	3-butylidene-7-hydroxyphthalide	203.1	12.5 <sup>b</sup>
9	30.78	neg	231.1358	231.1385	-1.2	C <sub>15</sub> H <sub>19</sub> O <sub>2</sub> <sup>-</sup>	Costunolide	231.1	3.02 <sup>b</sup>
10	31.20	neg	255.2295	255.2324	-1.1	C <sub>16</sub> H <sub>31</sub> O <sub>2</sub> <sup>-</sup>	Palmitic acid	255.2	2.40 <sup>b</sup>
11	15.93	pos	342.1728	342.1705	0.7	C <sub>20</sub> H <sub>24</sub> NO <sub>4</sub> <sup>+</sup>	Tetrahydrocolumbamine <sup>a</sup>	342.2	0.94
12	16.93	pos	354.1322	354.1341	-0.5	C <sub>20</sub> H <sub>20</sub> NO <sub>5</sub> <sup>+</sup>	Protopine <sup>a</sup>	354.1	1.63
13	17.89	pos	370.1617	370.1654	-1.0	C <sub>21</sub> H <sub>24</sub> NO <sub>5</sub> <sup>+</sup>	Allocryptopine	370.2	0.72 <sup>b</sup>
14	18.66	pos	324.1151	324.1236	-2.6	C <sub>19</sub> H <sub>18</sub> NO <sub>4</sub> <sup>+</sup>	Tetrahydrocoptisine <sup>a</sup>	324.1	0.83
15	19.17	pos	356.1862	356.1862	0	C <sub>21</sub> H <sub>26</sub> NO <sub>4</sub> <sup>+</sup>	Tetrahydropalmatine <sup>a</sup>	356.2	1.54
16	19.52	pos	356.1869	356.1862	0.2	C <sub>21</sub> H <sub>26</sub> NO <sub>4</sub> <sup>+</sup>	Glaucine	356.2	0.73 <sup>b</sup>
17	21.59	pos	370.2031	370.2018	0.4	C <sub>22</sub> H <sub>28</sub> NO <sub>4</sub> <sup>+</sup>	Corydaline <sup>a</sup>	370.2	7.92
18	22.17	pos	336.1205	336.1236	-0.9	C <sub>20</sub> H <sub>18</sub> NO <sub>4</sub>	Berberine <sup>a</sup>	336.1	0.82
19	22.87	pos	366.1655	366.1705	-1.4	C <sub>22</sub> H <sub>24</sub> NO <sub>4</sub>	Dehydrocorydaline <sup>a</sup>	366.2	8.64
20	28.91	pos	233.1542	233.1550	-3.4	C <sub>15</sub> H <sub>20</sub> NO <sub>2</sub>	Costuslactone	233.2	0.63 <sup>b</sup>

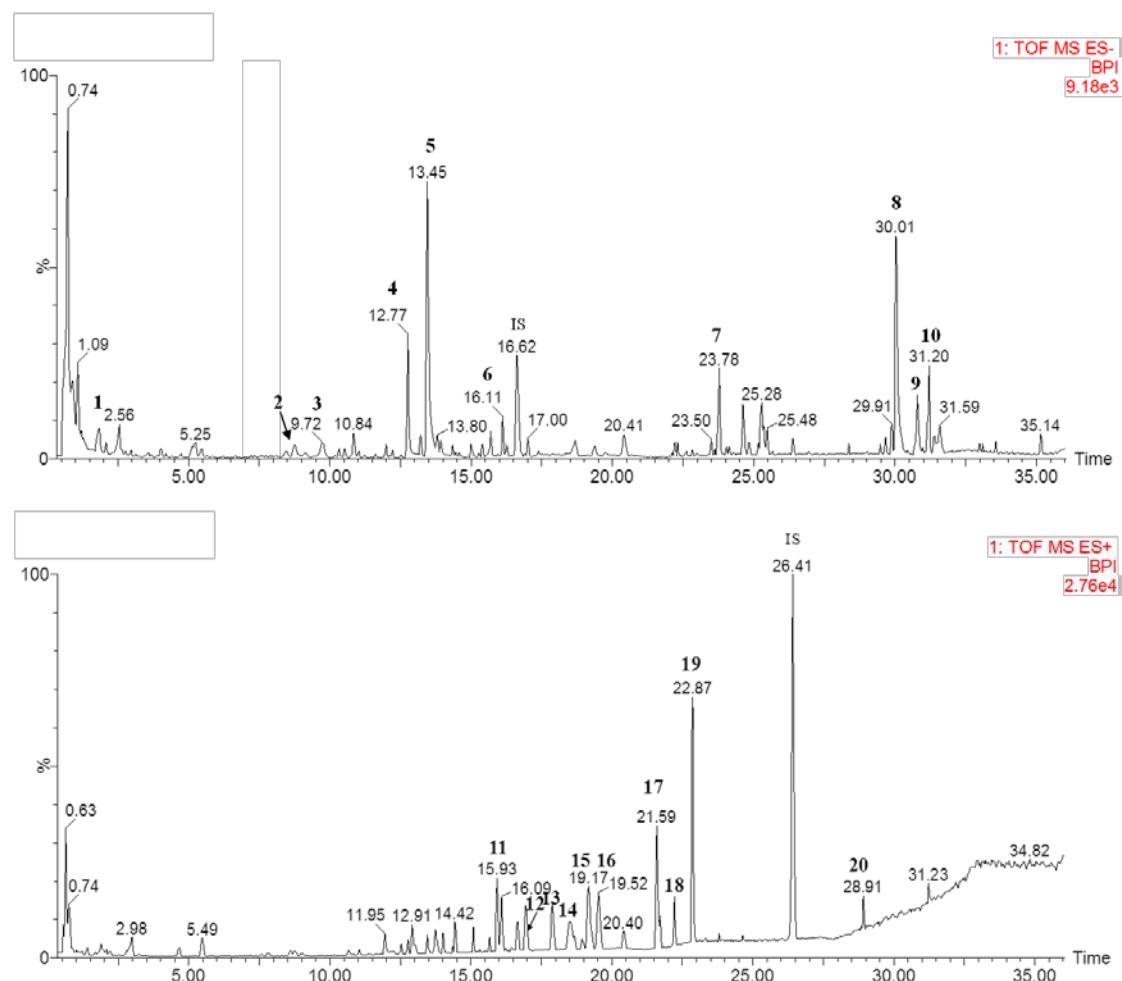
<sup>a</sup> Confirmed by reference compounds.

<sup>b</sup> Relative content to internal standard.

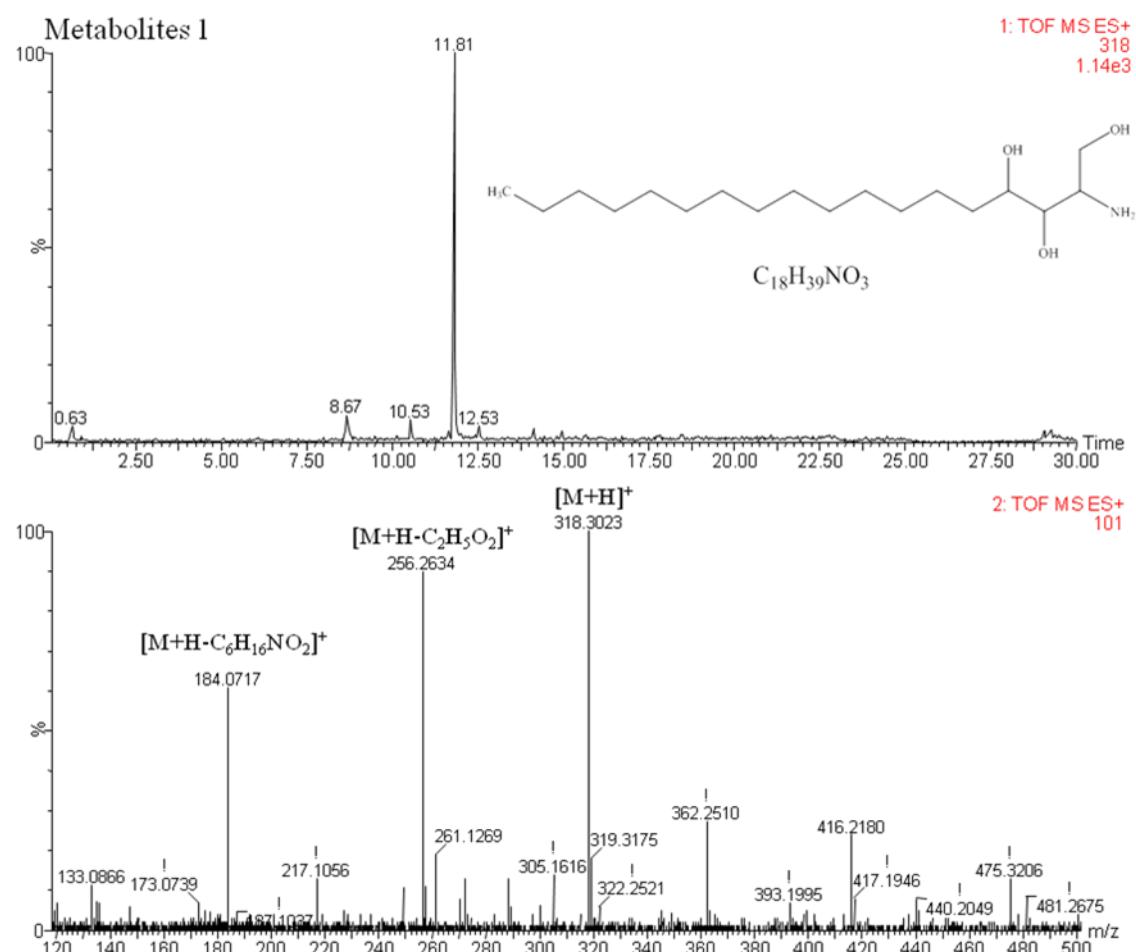
**Table 3S.** Precursor/product ion pairs and parameters for MRM of the marker compounds

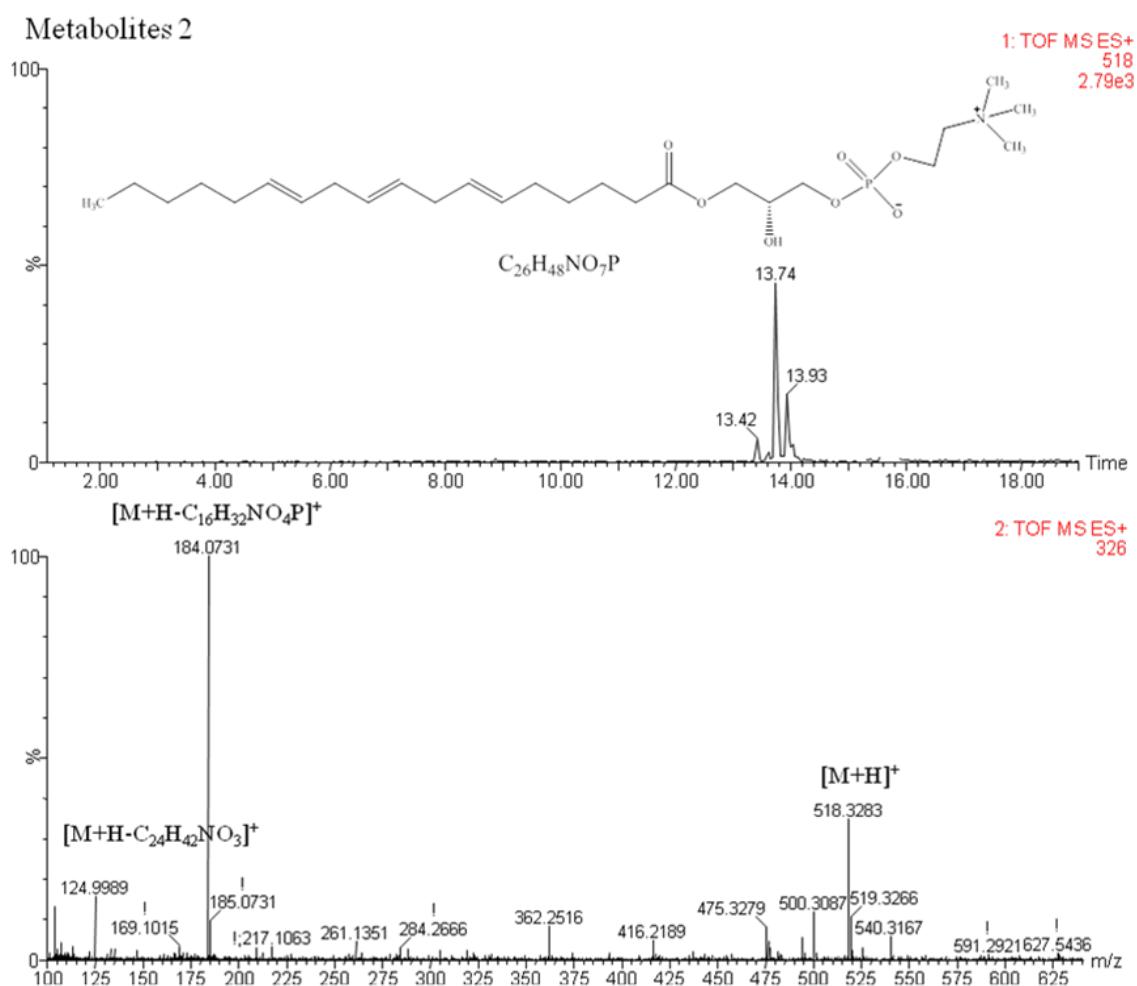
Analyte	Retention time (min)	[M + H] <sup>+</sup> (m/z)	MRM transitions (Precursor→product)	Cone voltage (V)	Collision energy (eV)
<b>1</b> Phytosphingosine	11.71	318.30	318.30→256.26	30	20
<b>2</b> LysoPC (18:3)	13.67	518.33	518.33→184.07	30	20
<b>3</b> LysoPC (16:1)	14.16	494.33	494.33→184.07	30	20
<b>4</b> LysoPC (20:4)	14.44	544.34	544.34→184.07	30	20
<b>5</b> LysoPC (18:2)	14.75	520.33	520.33→184.07	30	20
<b>6</b> LysoPC (16:0) <sup>b</sup>	15.64	496.34	496.34→184.07	30	20
<b>7</b> LysoPC (18:1)	16.05	522.36	522.36→184.07	30	20
<b>8</b> Estrone <sup>b</sup>	9.25	271.17	271.17→147.08	30	20
<b>9</b> 17-Hydroxyprogesterone	11.14	331.22	331.22→138.05	30	20
<b>10</b> Myristoylglycine	11.27	286.24	286.24→227.13	30	20
<b>11</b> Dihydrocortisol <sup>b</sup>	11.78	365.23	365.23→223.10	30	20
<b>12</b> Palmitoylglycine	12.78	314.27	314.27→255.16	30	20
<b>13</b> Phytosphingosine	13.75	318.30	318.30→184.07	30	20
<b>14</b> Sphingosine	15.15	338.24	338.24→281.23	30	20
<b>15</b> LysoPC (10:0)	16.74	413.26	413.26→184.07	30	20
<b>16</b> IS	9.69	748.48	748.48→158.96	30	20

**Figure 1S.** UPLC - ESI- MS base peak intensity (BPI) chromatograms at the positive and negative ion mode of Xiang-Fu-Si-Wu Formula

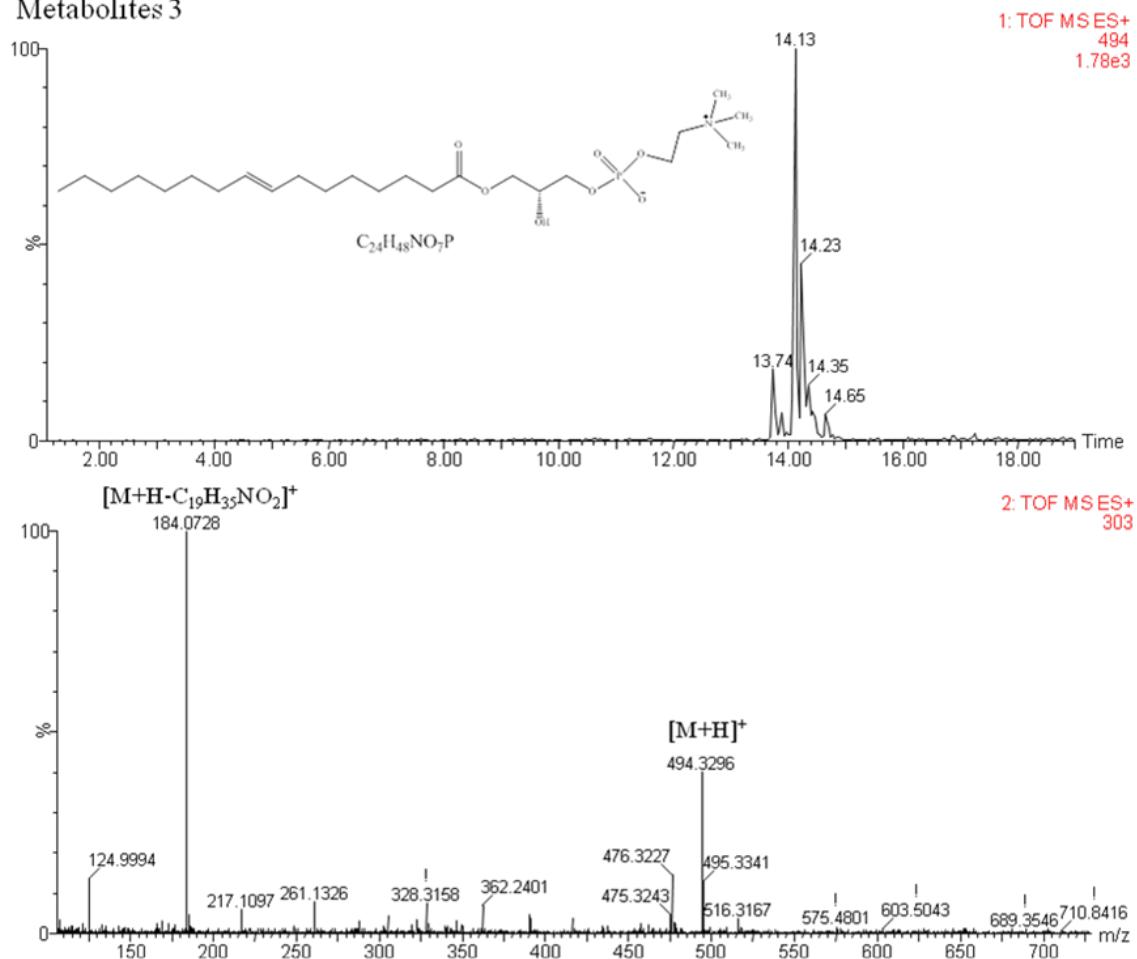


**Figure 2S.** Peak and corresponding mass spectrum of potential markers (Metabolites 1-15).

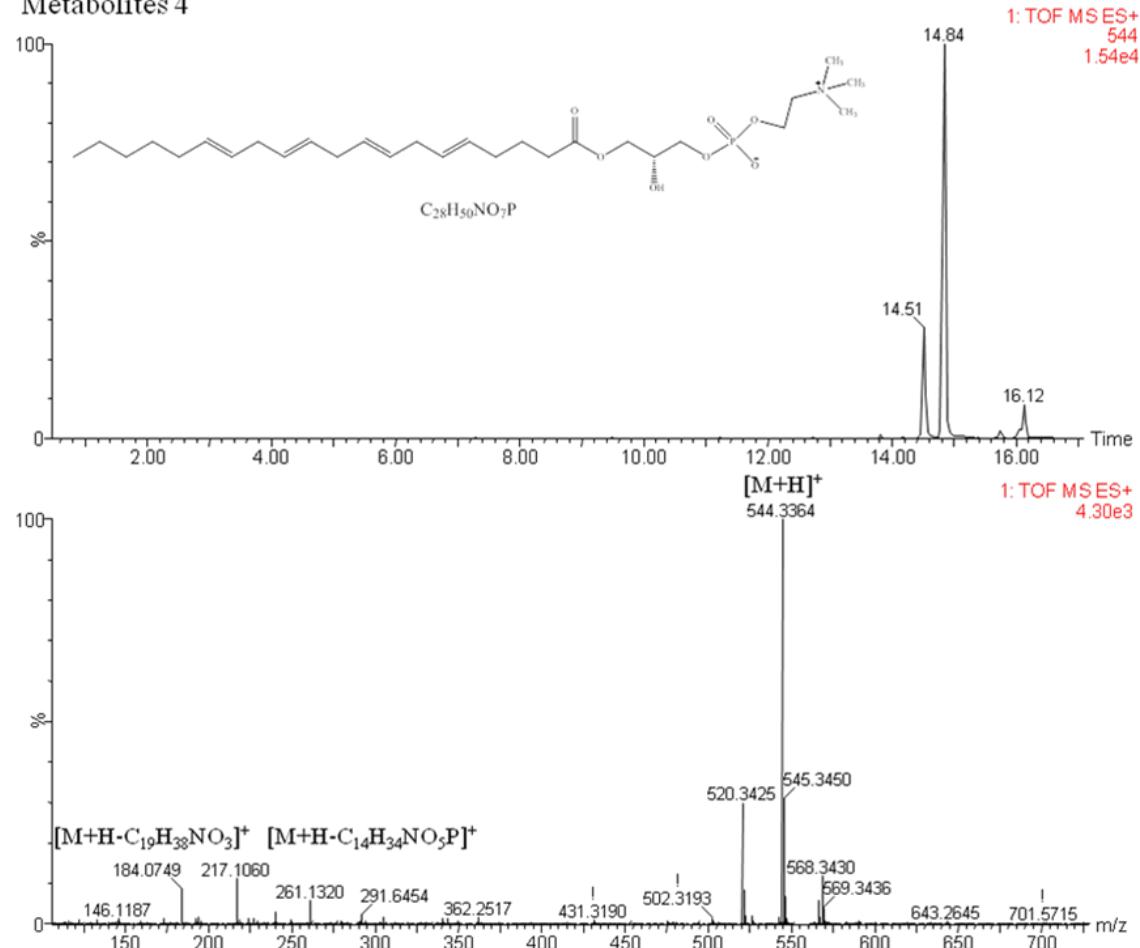




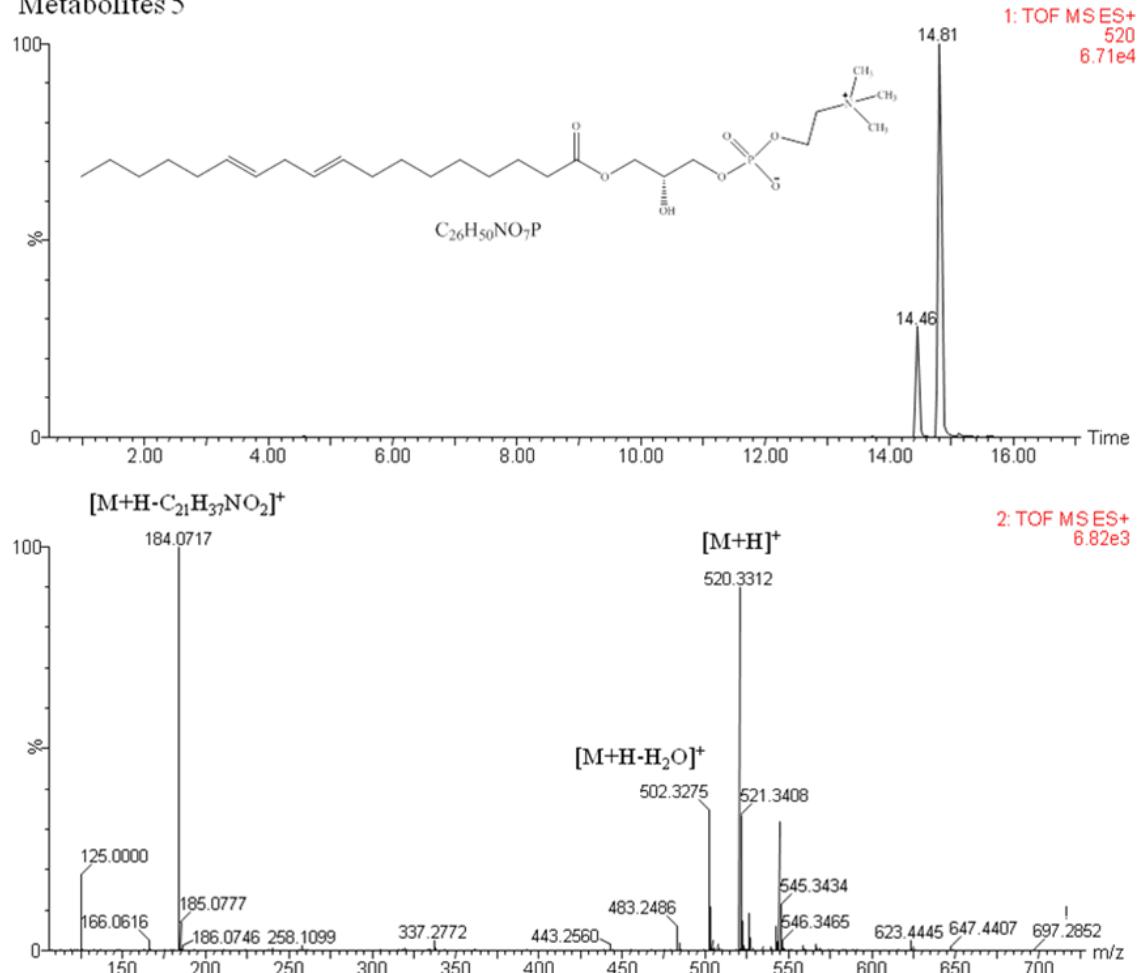
Metabolites 3



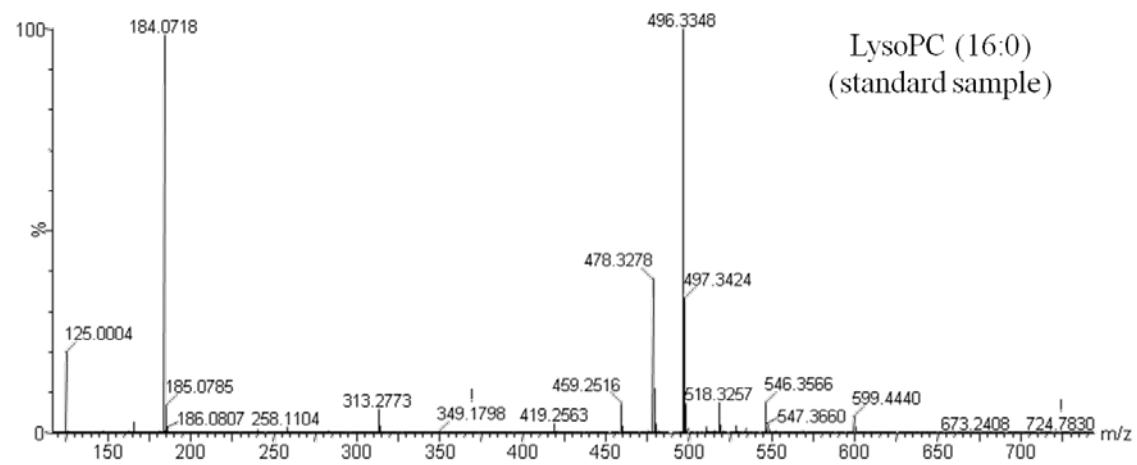
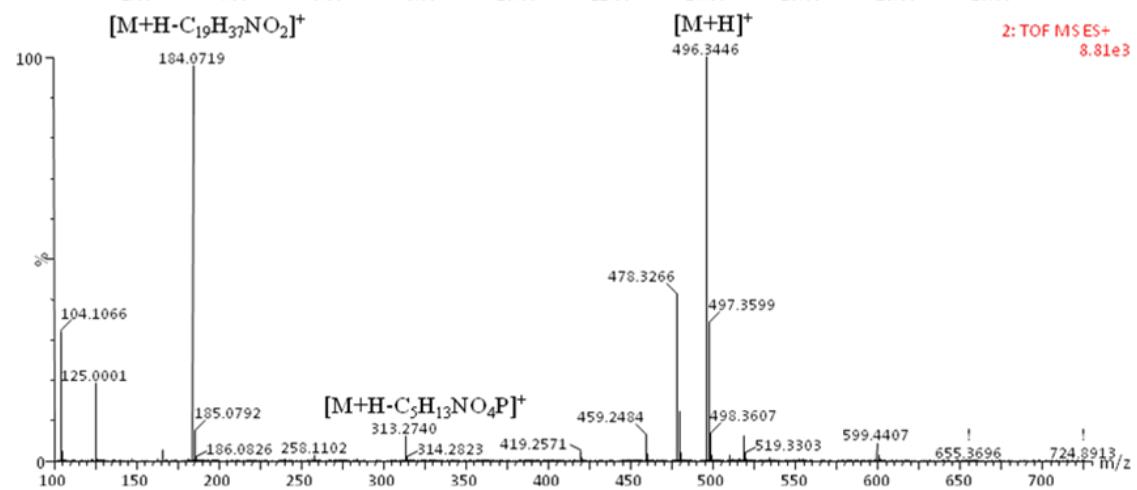
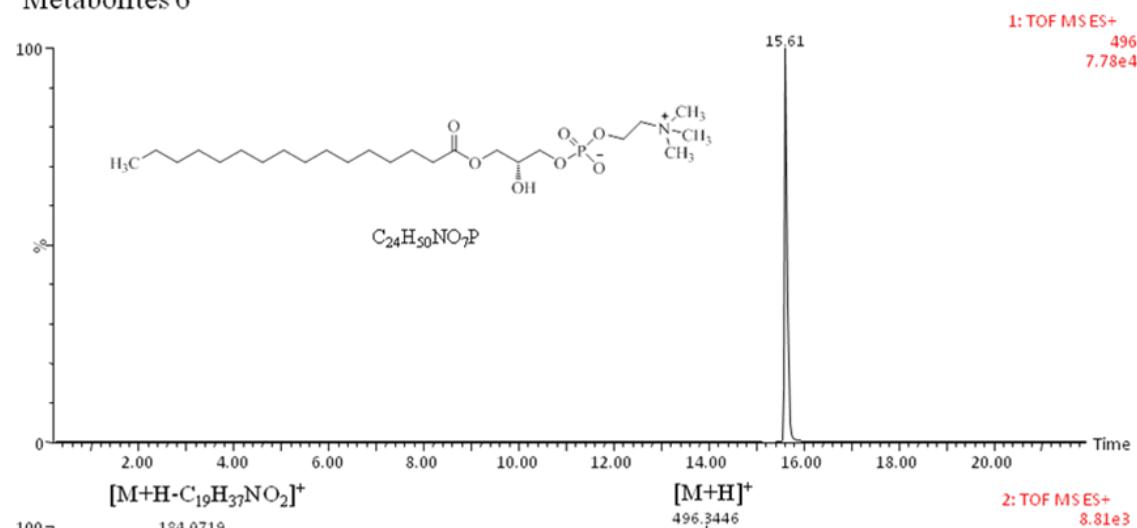
Metabolites 4

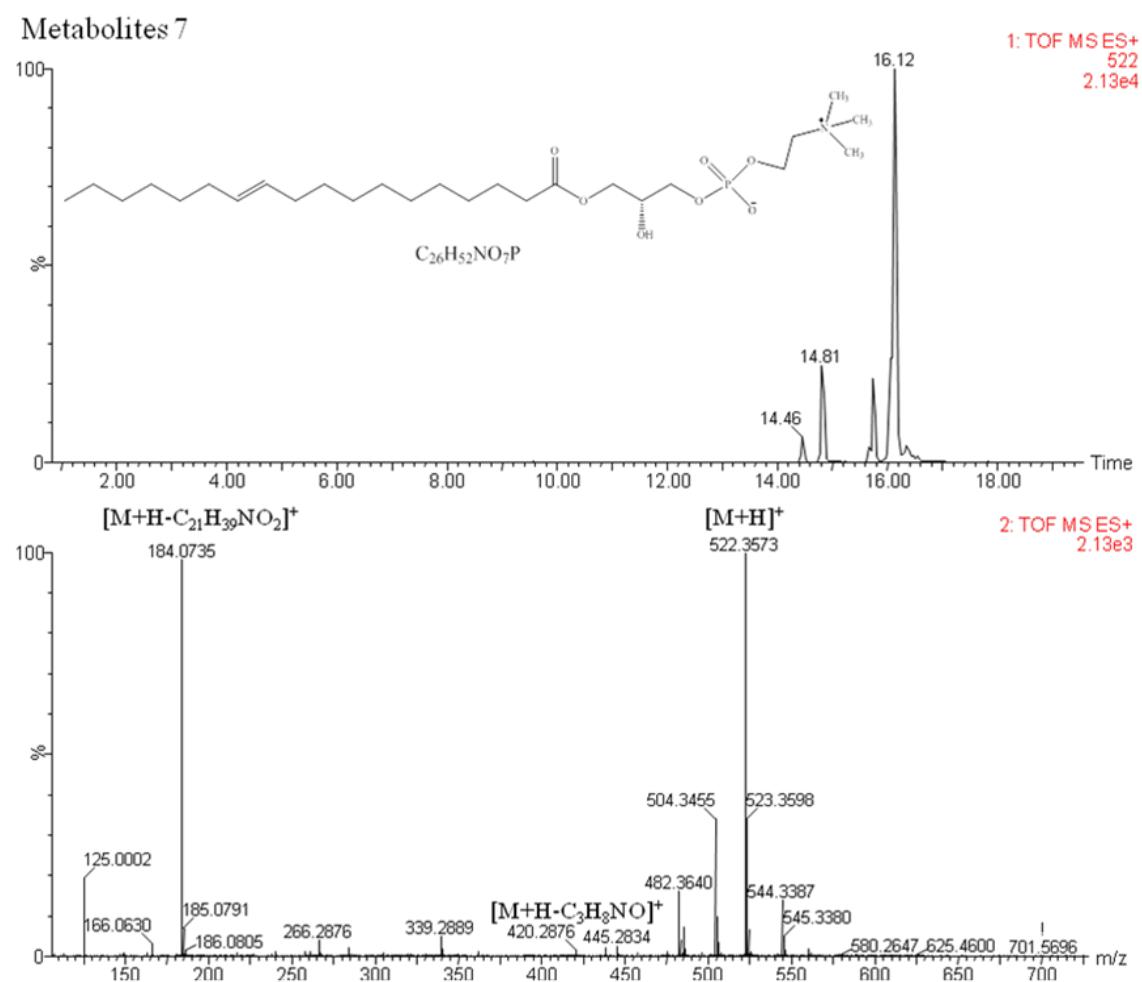


Metabolites 5



Metabolites 6





Metabolites 8

