Electronic Supplementary Information

Analyte Migration Electrospray Ionization for Rapid Analysis of Complex Samples with Small Volume Using Mass Spectrometry

Qian Wang,[a] *Hanbin Zhong,*[a] *Yajun Zheng,*[a] *Sichun Zhang,*[b] *Xiaoning Liu,*[a] *Xinrong Zhang,*[b] *Xiaoling Zhang*[a] *and Zhiping Zhang** [a]

[a] School of Chemistry and Chemical Engineering, Xi'an Shiyou University, Xi'an 710065, China

[b] Department of Chemistry, Tsinghua University, Beijing 100084, China

*Corresponding authors.

zhangzp0304@gmail.com (Z.Z.)

Experimental Section

All experiments were carried out with a TSQ Quantum Access Max (Thermo Scientific, San Jose, CA), operated in the full mass spectrum mode or selected reaction monitoring (SRM) mode, was used. The specific product ions produced by collision-induced dissociation (CID) were monitored. The Xcalibur software was used for control of the TSQ Quantum Access Max MS system and data acquisition. Argon gas (99.995% purity) was used as collision gas. The temperature MS inlet capillary was 270 ℃. The AM-ESI capillary with various tip orifices were pulled from borosilicate glass capillaries with filament (Sutter Instrument, USA, 1.5 mm o.d., 0.86 mm i.d., 10 cm length) using a micropipette puller (Model P-97, Sutter Instrument Co., Novato. CA, USA). The tip orifice was determined with a metallographic microscope equipped with a DCA 10.0 digital camera (1 million resolution). The orifice precision was ± 1 μm. The tip orifice size of 1-35 μm was obtained by adjusting the pulling parameters. The procedure for paper spray analysis was similar to the previous reports.[S-1] The paper used was Grade 1 chromatography paper purchased from Whatman (Maidstone, England). The blood used was bovine whole blood from Lanzhou Institute of Biological Products Co., Ltd. (Lanzhou, China). For the AM-ESI experiment, the distance between the tip of capillary and MS inlet should be well controlled, and the used distance is around 8 mm. The selected reaction monitoring (SRM) conditions for the quantitative analysis of different drugs in the whole blood is listed in Table S-1.

References:

[S-1] (a) H. Wang, J. Liu, R. G. Cooks, Ouyang, Z., *Angew. Chem. Int. Ed.* **2010,** *49* (5), 877-880; (b) Z. Zhang, W. Xu, N. E. Manicke, R. G., Cooks, Ouyang, Z., *Anal. Chem.* **2012,** *84* (2), 931-938.

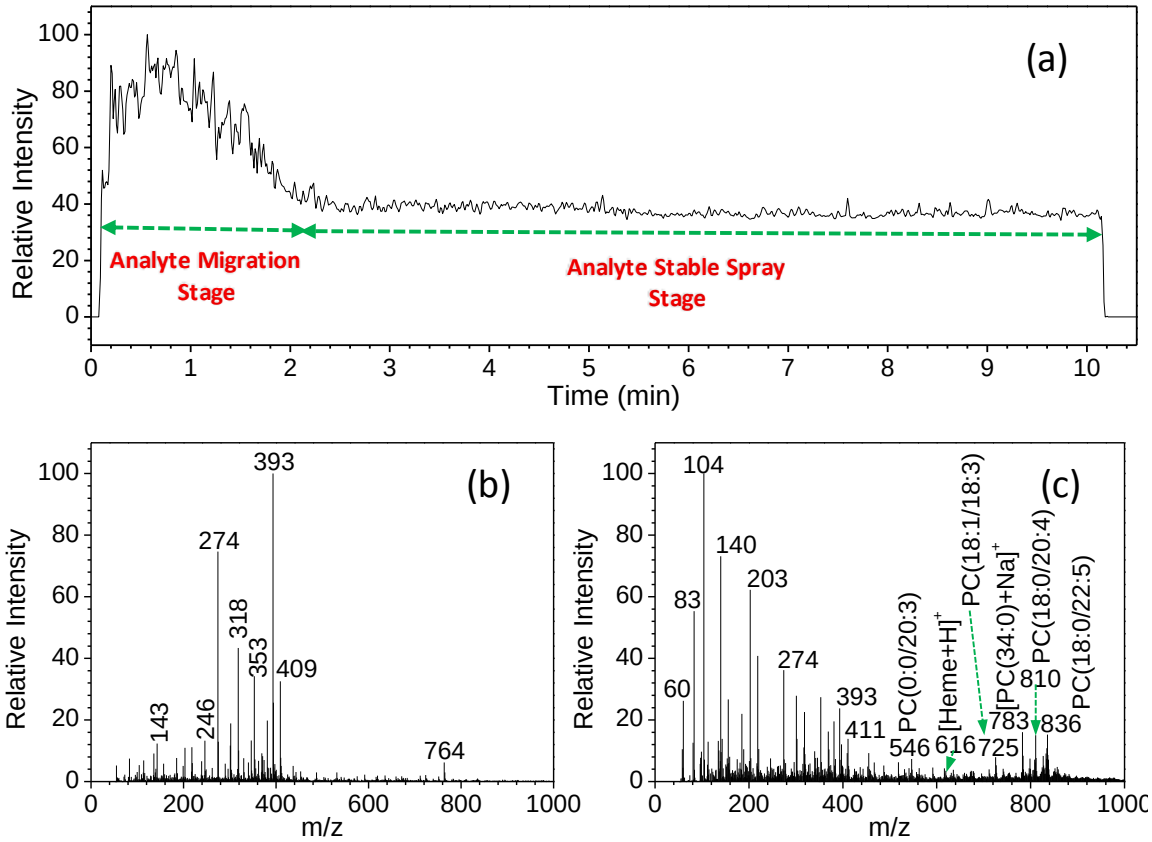

Fig. S-1 (a) The total ion current chronogram of fresh blood sample with AM-ESI by applying 2 kV voltage. It includes Analyte Migration Stage and Analyte Stable Spray Stage. The capillary with 20 μm tip orifice containing 2 μL fresh blood and 20 μL methanol before spray, and the blood sample was added into the end of methanol as Figure 1b in the main text. (b) The mass spectrum from the Analyte Migration Stage as shown in (a). The peaks could be assigned as the products from methanol. (c) The mass spectrum from the Analyte Stable Spray Stage as shown in (a). (Note: PC means phosphatidylcholine in (c).)

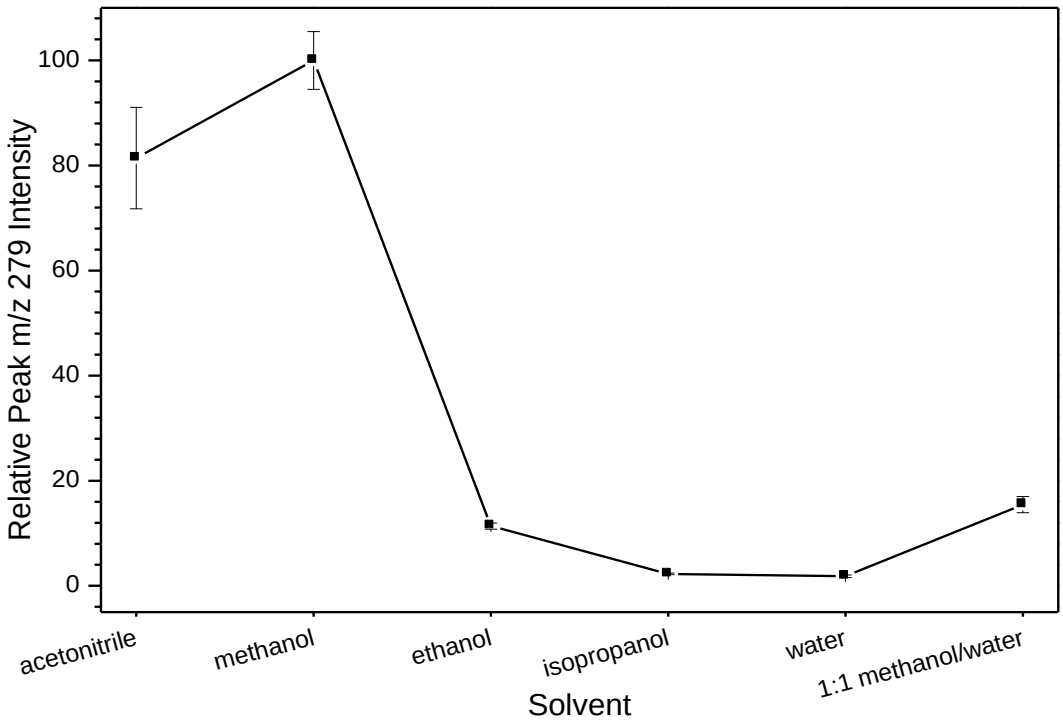

Fig. S-2 Effect of solvent on the extraction efficiency for analysis of olive oil by AM-ESI, and the peak intensity was evaluated by the peak m/z 279 (linoleic acid) in olive oil. For this analysis, 2 μL olive oil sample was added into a capillary containing 20 μL methanol, and then -1.5 kV DC voltage was applied.

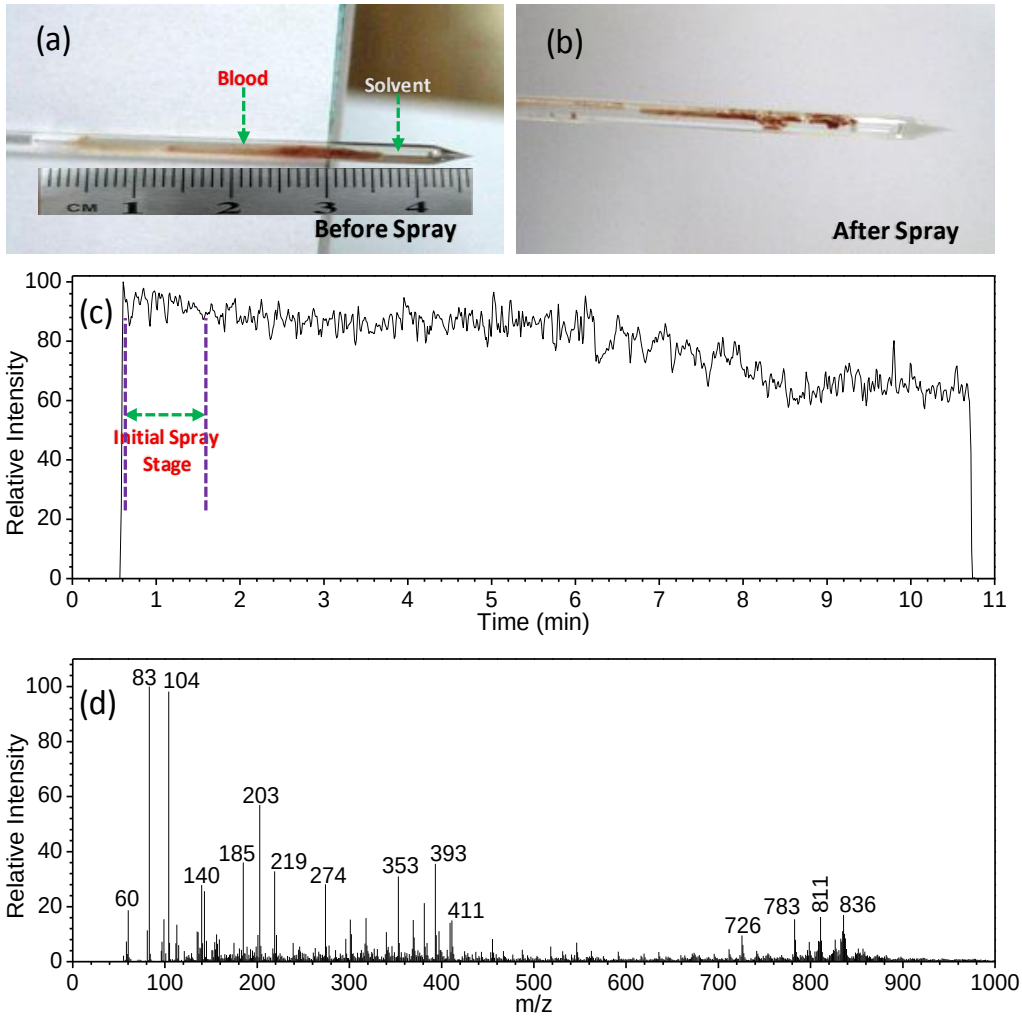

Fig. S-3 (a) The capillary with 20 μm tip orifice containing 2 μL fresh blood and 20 μL methanol before spray, and the blood sample was added into the solvent methanol 4 - 6 mm away from the capillary tip. (b) The capillary after spray for ca. 10 min. (c) The total ion current chronogram of fresh blood sample with AM-ESI by applying 2 kV voltage. (d) The mass spectrum from the Initial Spray Stage as shown in (c).

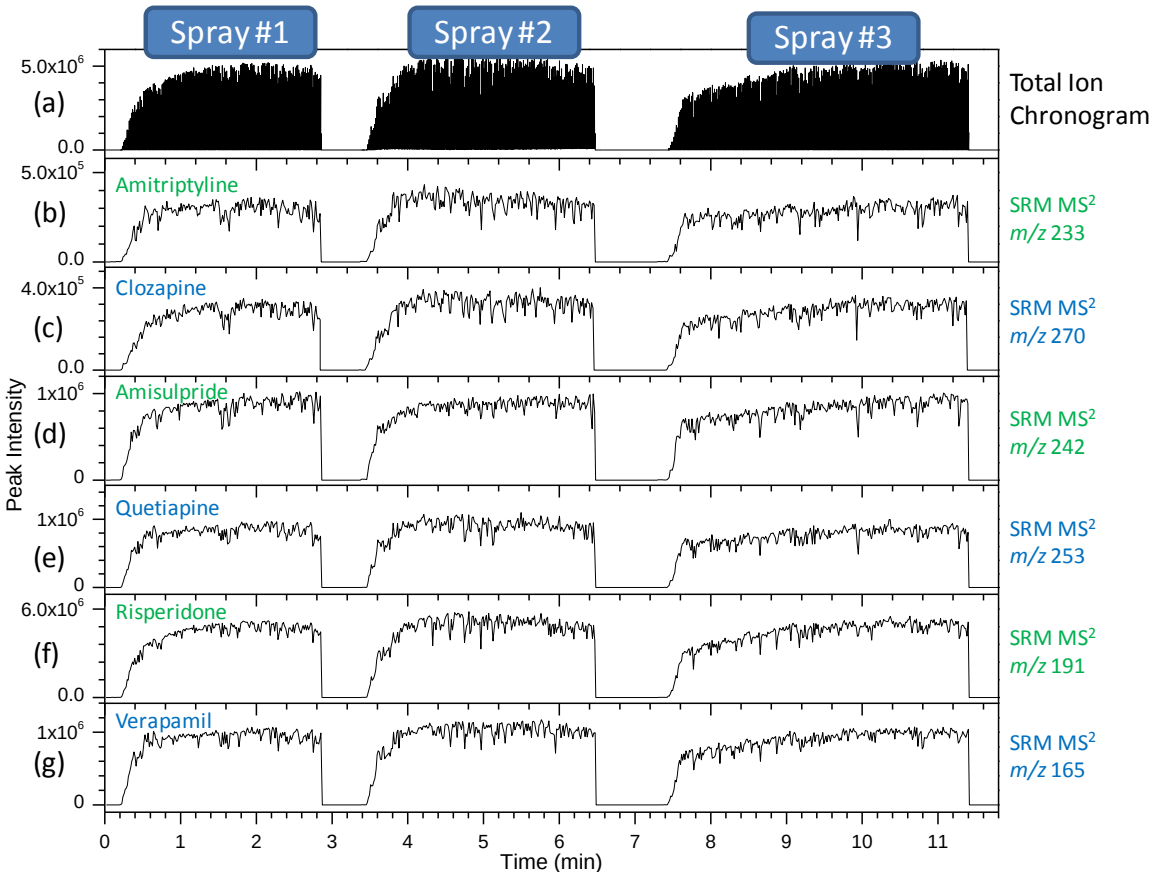

Fig. S-4 Simultaneous determination of six therapeutic drugs in fresh blood using AM-ESI. Ion chronograms for (a) total ion curent (TIC) and (b) amitriptyline, (c) clozapine, (d) amisulpride, (e) quetiapine, (f) risperidone and (g) verapamil, each at 1 μg mL^{-1} concentration in fresh blood, and selected reaction monitoring (SRM) mode of a Thermo TSQ. Sample amount: 2 μL; solvent: methanol; solvent volume: 20 μL; voltage: 2.0 kV.

Fig. S-4 shows the simultaneous determination of six therapeutic drugs in fresh blood using AM-ESI ionization source coupled to mass spectrometry. It is obvious that AM-ESI not only benefits from without sample preparation, but also from high-throughput analysis. Also, the analysis repeatability is good enough. The analysis time was mainly spent on the changing of sample, and the sample spray time can be easily adjusted dependent on the real requirement.

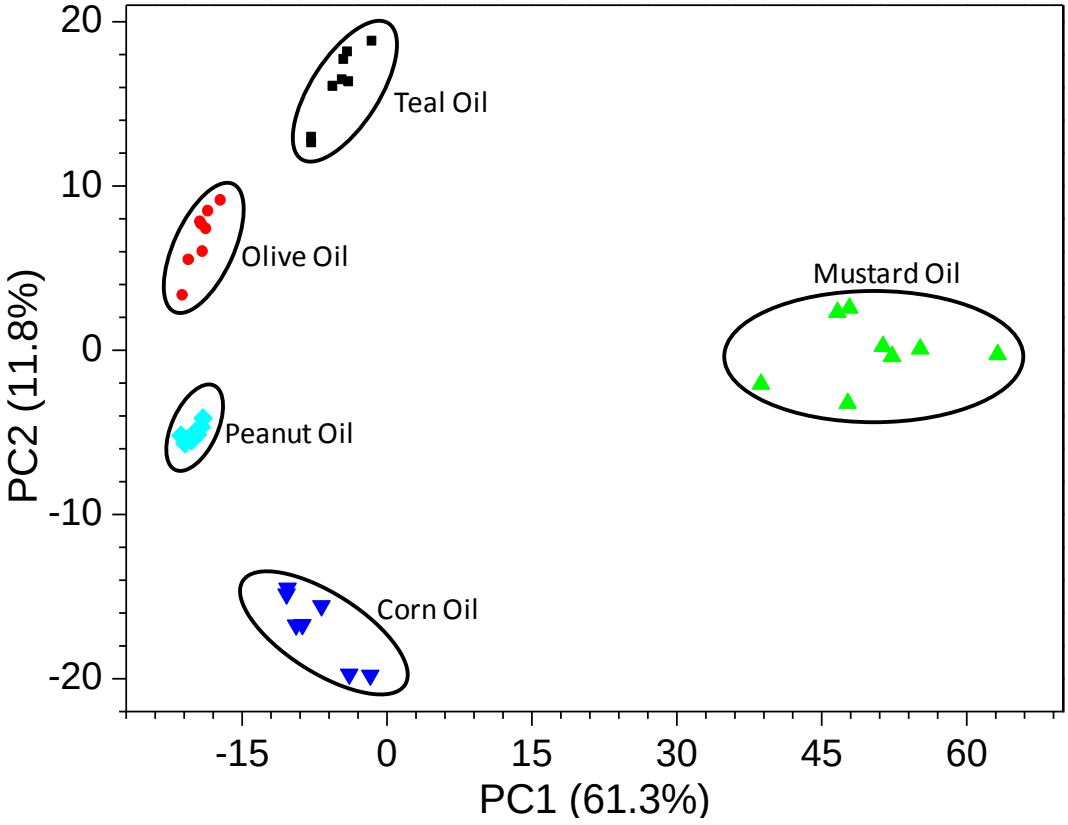

Fig. S-5 PCA of AM-ESI-mass spectrometry of five oil samples including teal oil, olive oil, peanut oil, corn oil, and mustard oil. For this analysis, 2 μL olive oil sample was added into a capillary containing 20 μL methanol, and then -1.5 kV DC voltage was applied.

Fig. S-5 shows the differential PCA score plot from the all data points in the m/z range of 50-1,200 from five types of oil samples (8 individual samples), demonstrating the feasibility of AM-ESI-mass spectrometry for rapid discrimination of the different oil samples. Although all data points from the mass spectra of teal oil, olive oil, peanut oil, corn oil, and mustard oil were used, the studied five oil samples can be well descriminated. It suggests that AM-ESI-mass spectrometry can produce abundant fingerprint information of different oils, which effectively aviods the cumbersome selection of the major different peaks for PCA analysis.

Table S-1. Selected reaction monitoring (SRM) conditions

Analyte	Parent Ion m/z	Fragment Ion *m/z*	Tube Lens (V)	q2 Offset (V)
Amitriptyline	278, $[M + H]^+$	233	16	73
Clozapine	327, $[M + H]^+$	270	23	80
Amisulpride	370, $[M + H]^+$	242	27	87
Quetiapine	384, $[M + H]^+$	253	22	89
Risperidone	411, $[M + H]^+$	191	27	93
Verapamil	455, $[M + H]^+$	165	26	107

Table S-2. Comparison of the LOQs of different therapeutical drugs in blood samples determined using AM-ESI and PSI ionization sources coupled to TSQ mass spectrometry

Analyte	AM-ESI ($ng\ mL^{-1}$)	PSI ($ng\ mL^{-1}$)
Amitriptyline	0.5	5.0
Clozapine	0.1	1.0
Amisulpride	0.5	5.0
Quetiapine	0.5	5.0
Risperidone	0.5	1.0
Verapamil	0.5	5.0

Table S-3. Assignment of the main peaks from olive oil from the data in the literature[S-2]

m/z	Compound
121	[tyrosol + H - H_2O]$^+$
137	[hydroxytyrosol +H – H_2O]$^+$
165	[coumaric acid + H]$^+$
181	[caffeic acid + H]$^+$
195	[ferulic acid + H]$^+$
225	[sinapic acid + H]$^+$
603	LO
645	OO
851	PPO
875	PLO
877	PLL
879	PLO
899	LLLn
901	LLL
903	LLO
905	OOL
908	OOO
910	SOO
912	SSO

Note: L denotes linoleic acid; O denotes oleic acid; P denotes palmetic acid; S denotes steric acid.

References:

[S-2] (a) R. R. Catharino, R. Haddad, L. G. Cabrini, I. B. S. Cunha, A. C. H. F. Sawaya, M. N. Eberlin, *Anal. Chem.* **2005**, *77*, 7429-7433; (b) R. Goodacre, S. Vaidyanathan, G. Bianchi, D. B. Kell, *Analyst* **2002**, *127*, 1457-1462; (c) J. O. Lay, R. Liyanage, B. Durham, J. Brooks, *Rapid Commun. Mass Spectrom.* **2006**, *20*, 952-958.

Table S-4. Assignment of the main peaks from porcine kidney from the data in the literature[S-3]

m/z	Compound
255	[palmitic acid – H]$^-$
279	[linoleic acid – H]$^-$
281	[oleic acid – H]$^-$
303	[arachidonic acid –H]$^-$
722	plasm-PE
738	PE(36:4)
766	PE(38:4)
810	PS(38:4)
861	PI(36:2)
885	PI(38:4)

Note: plasm-PE denotes plasmalogens; PE denotes glycerophosphoethanolamines; PS denotes phosphatidylserine; PI denotes phophatidylinositol.

References:

[S-3] J. Liu, R. G. Cooks, Z. Ouyang, *Anal. Chem.* **2011**, *83*, 9221-9225.

Table S-5. Assignment of the main peaks from human hair from the data in the literature[S-4]

m/z	Compound
512	N14DS18
528	A14DS18
536	A16S18
538	N16:1DS18
540	N16DS18
548	N18S18
568	N18DS18
576	N20S18
596	N18DS20
636	N23:1DS18
660	N26S18
678	N26:1DS18
706	N28:1DS18
708	N28DS18
734	N30:1DS18

Note: The composition of ceramides (CERs) in hair is characterized not only by predominant CER molecules consisting of saturated/unsaturated fatty acid moietys (FAMs) with even numbers of carbon atoms and a C_{18} dihydrosphingosine moiety but also by isobaric or isomeric CERs, α-hydroxy fatty acid-containing CERs, and odd chain-ontaining CERs. FAM and a dihydrosphingosine moiety (ADS), or a α-hydroxy FAM and a sphingosine moiety (AS). Based on this terminology, each CER molecule is individually termed as follows: the number of FAM carbon atoms and unsaturation (if present) is expressed after the letter N or A, whereas the number of SPM carbon atoms is expressed after the letter(s) DS or S (e.g., N24:1DS18 for a CER molecule with nervonic acid and C_{18} dihydrosphingosine moieties, N18DS20 for stearic acid and C_{20} dihydrosphingosine, and A16DS18 for α-hydroxypalmitic acid and C_{18} dihydrosphingosine).

References:

[S-4] (a) Y. Masukawa, H. Tsujimura, H. Narita, *J. Lipid Res.* **2006**, *47*, 1559-1571; (b) Y. Masukawa, H. Tsujimura, *J. Chromatogr. A* **2006**, *1127*, 52-59.