

Fig. 4 Product ion spectra of putative IQ-C8-dG (A) and IQ-N⁶-dA (B). The cone voltages and collision energies were set at 15 V and 20-60 eV in the positive ion mode, respectively.

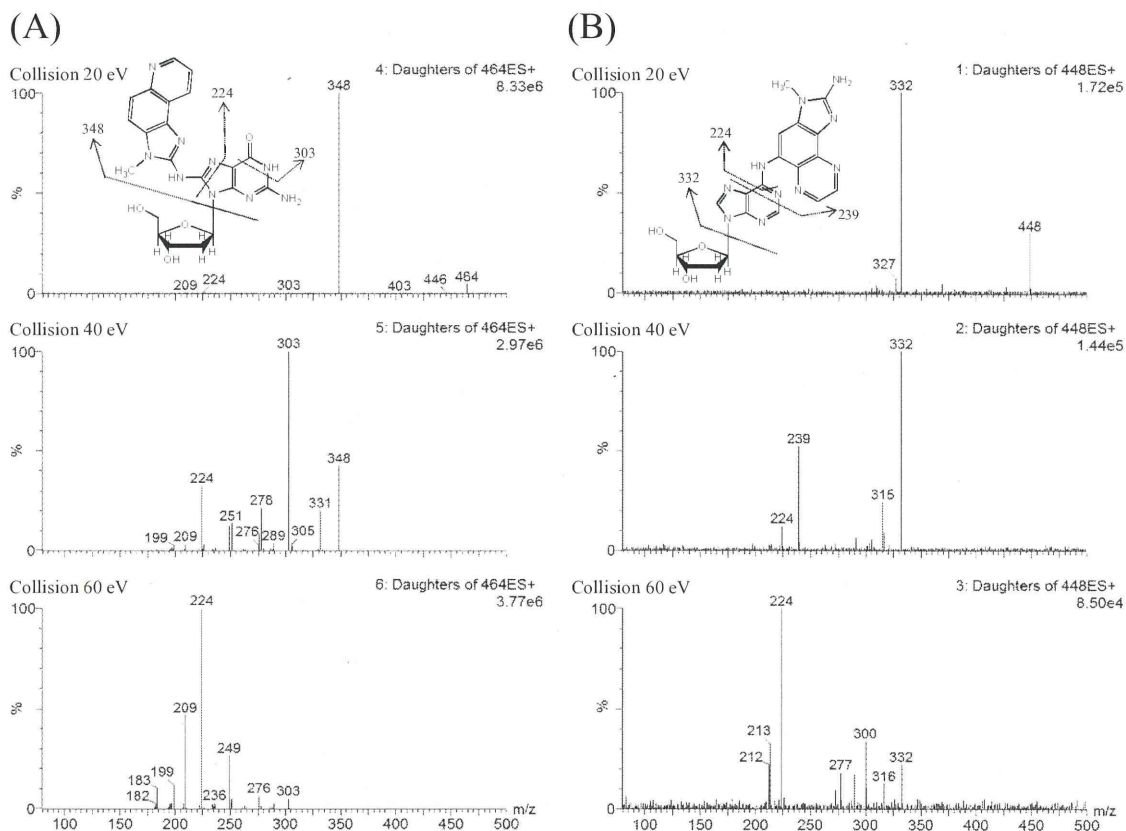


Fig. 5 Representative MRM chromatograms of the IQ- (A) or SFO- (B) induced putative DNA adducts in the livers and kidneys of F344 *gpt* delta rats

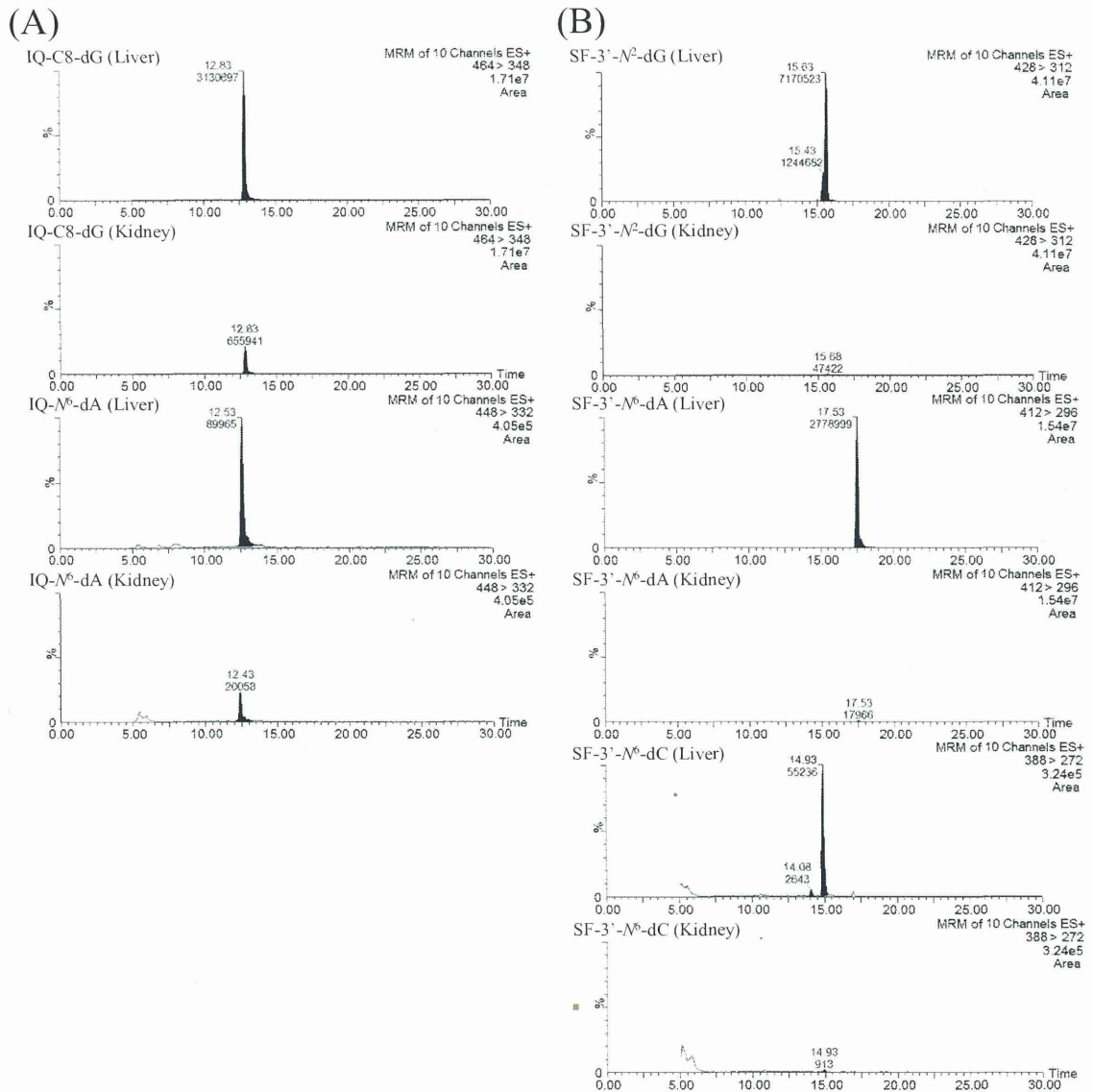


Fig. 6 DNA adductome maps of Liver (A) and kidney (B) of rats treated with SFO for 4 weeks. Black and blue spots are indicating control and SFO-treated rats, respectively. Red spots are indicating putative IQ-specific DNA adducts.

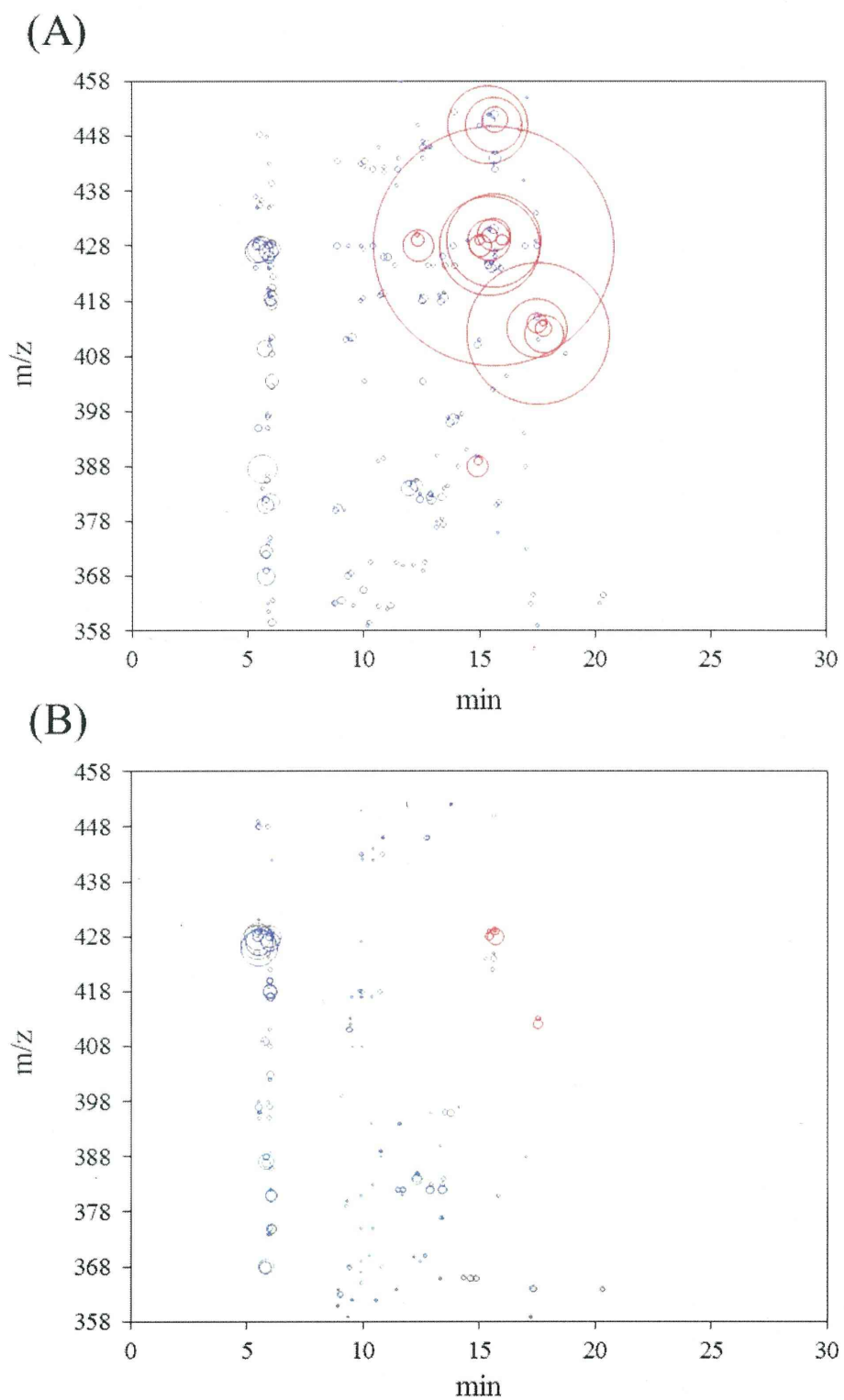


Fig. 7 Product ion spectra of putative SFO-3'-N²-dG (A) and SFO-3'-N⁶-dA (B). The cone voltages and collision energies were set at 15 V and 20-60 eV in the positive ion mode, respectively.

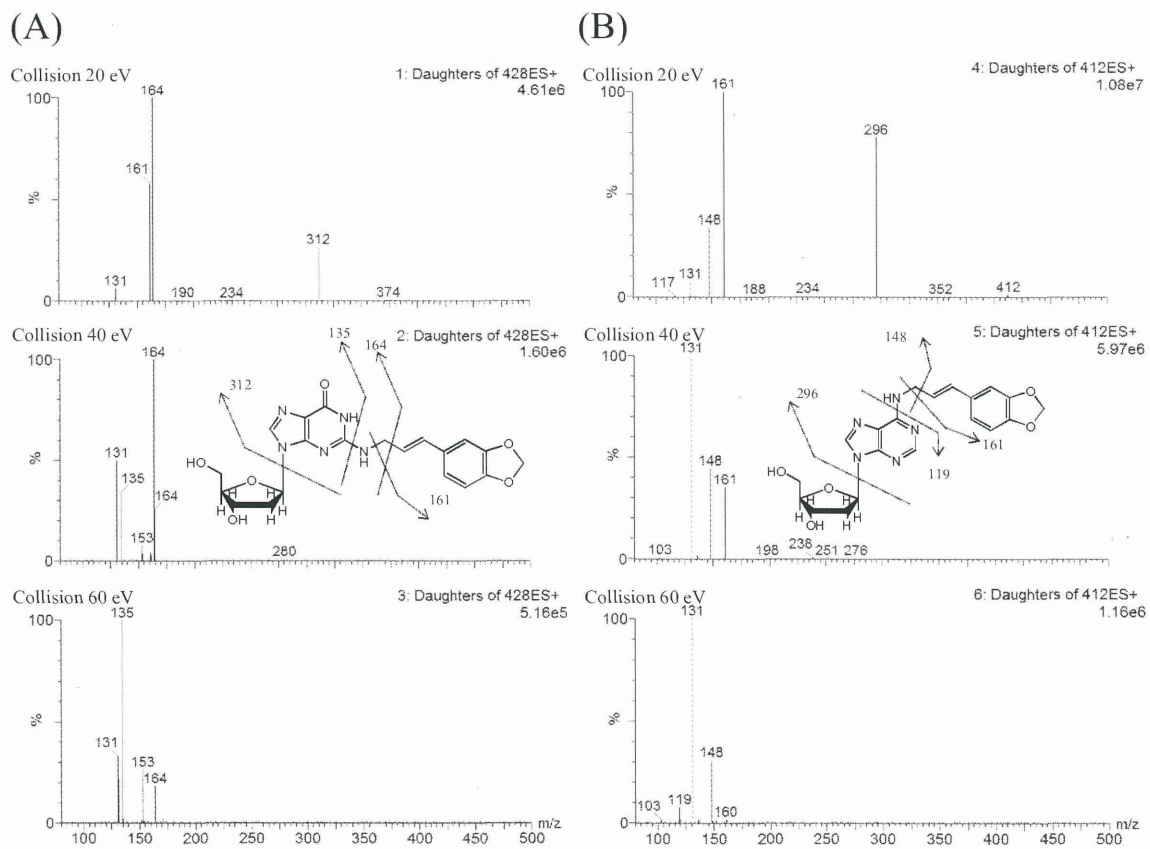


Fig. 8 DNA adductome maps of Liver (A) and kidney (B) of rats treated with Alz for 4 weeks. Black and orange spots are indicating control and Alz-treated rats, respectively.

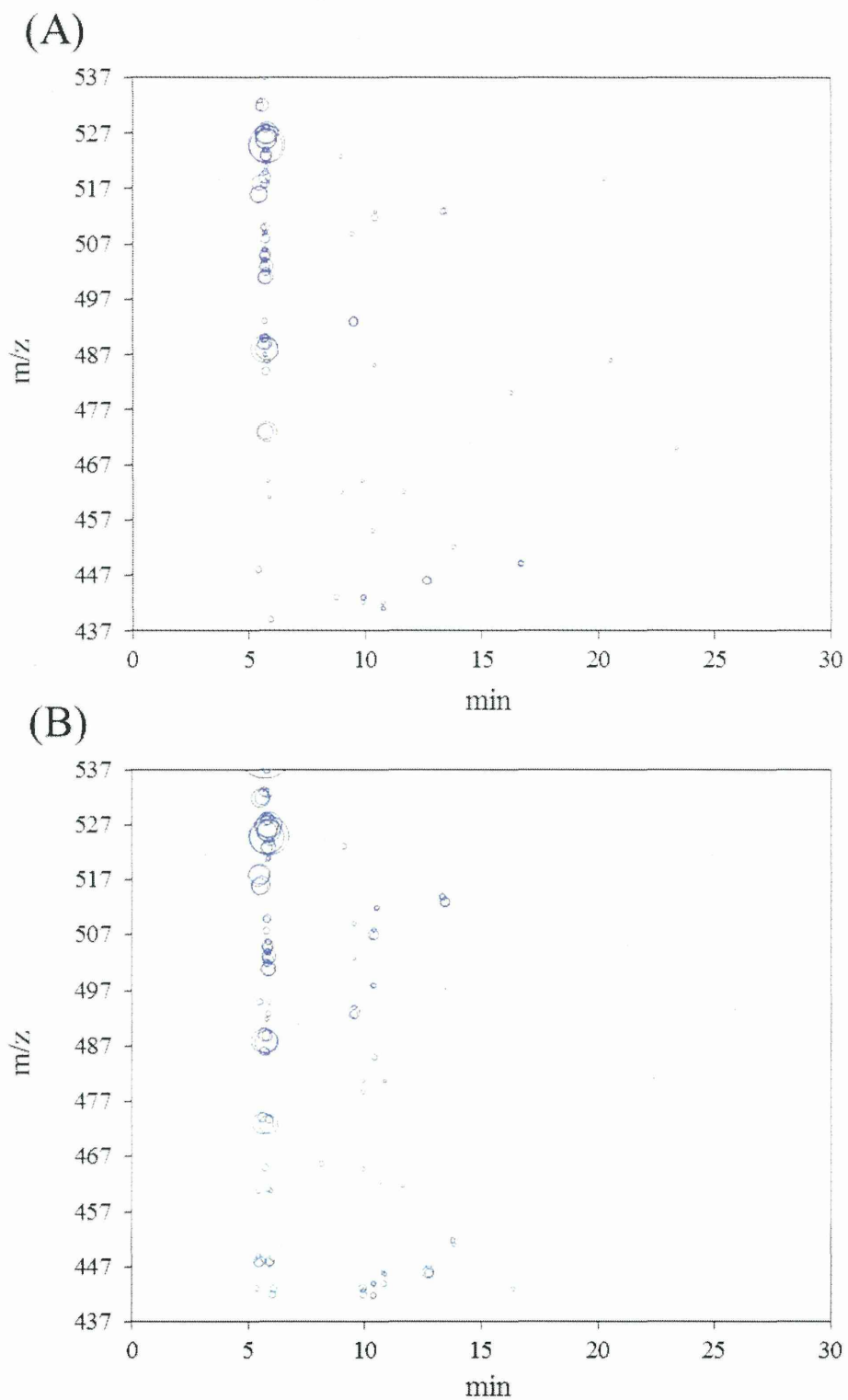


Fig. 9 DNA adductome maps of liver (A) and kidney (B) of rats treated with ES for 4 weeks. Black and blue spots are indicating control and ES-treated rats, respectively. Red spots are indicating putative ES-specific DNA adducts.

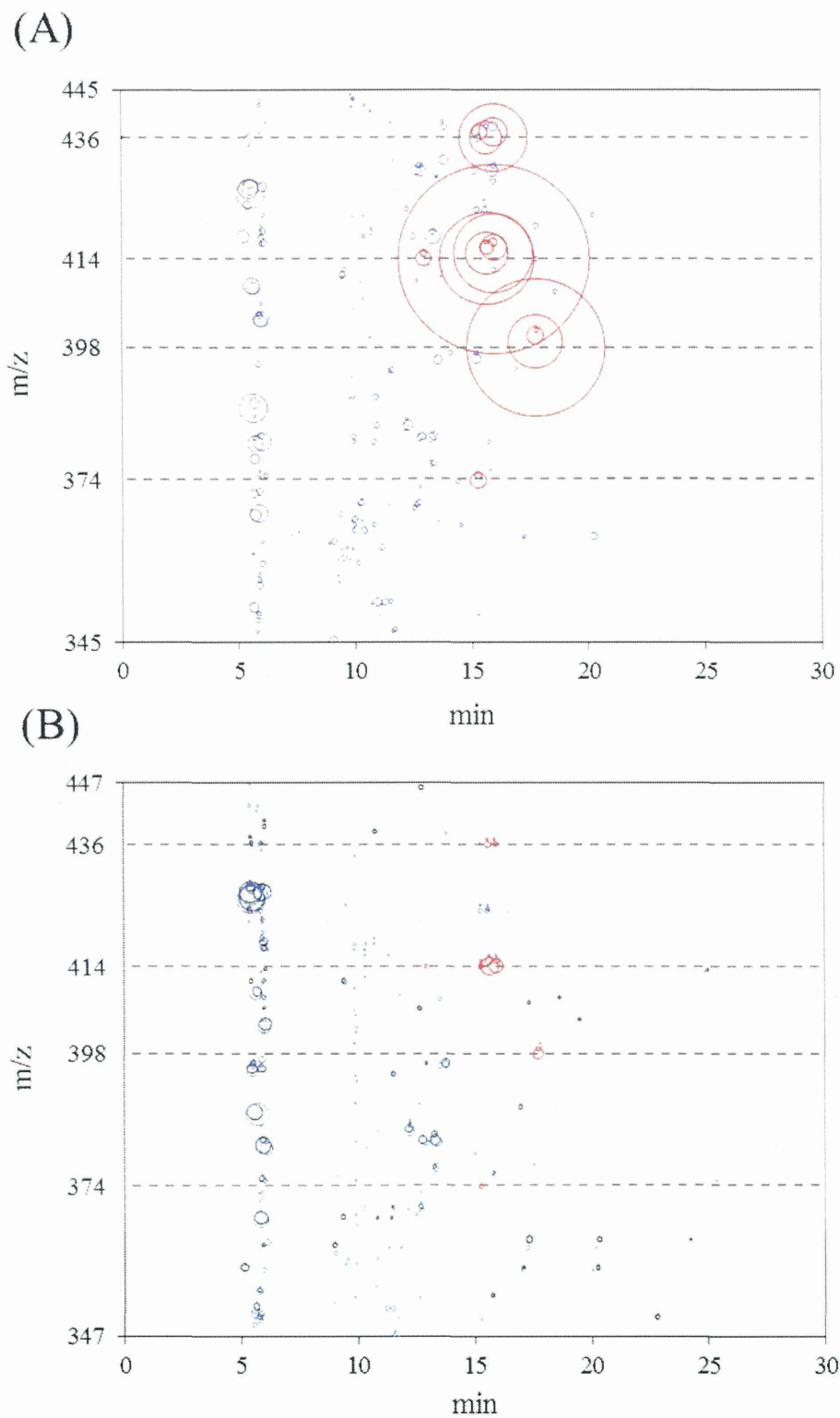


Fig. 10 Representative MRM chromatograms of the ES- (A), MEG- (B) or EG- (C) induced putative DNA adducts in the livers and kidneys of F344 *gpt* delta rats

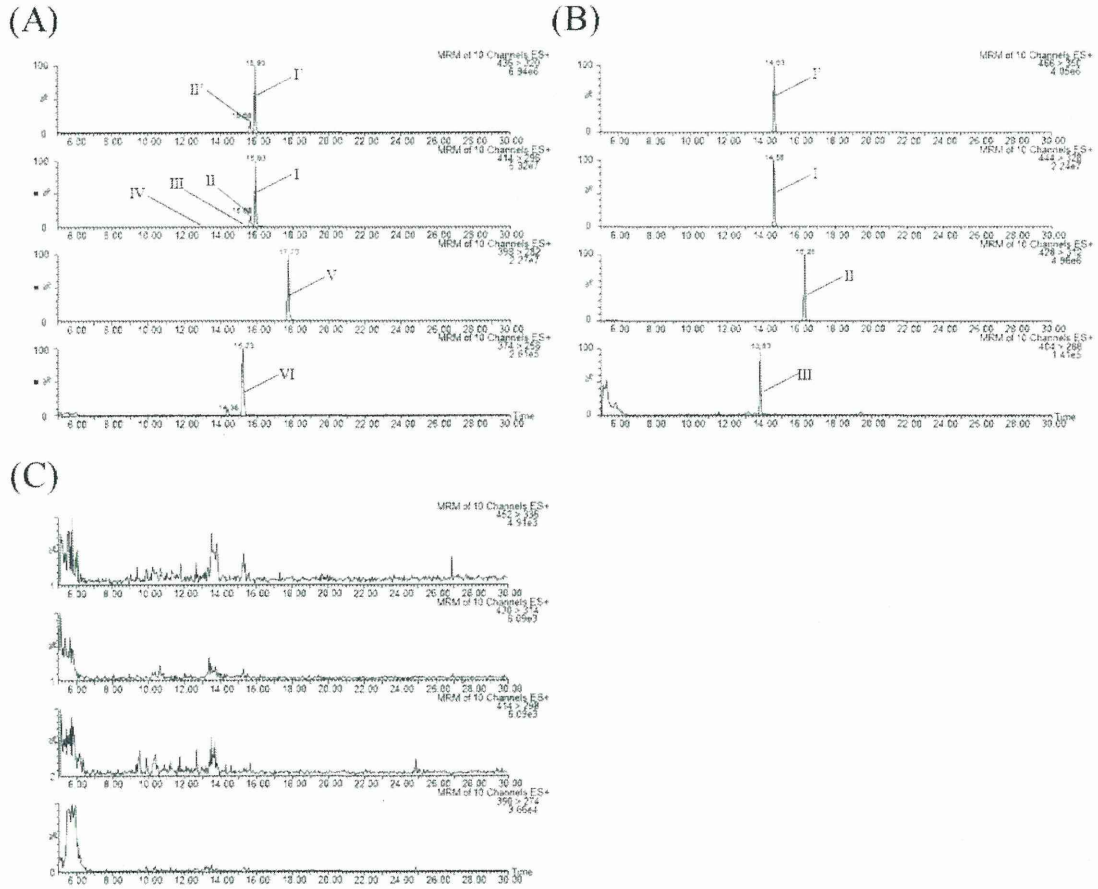
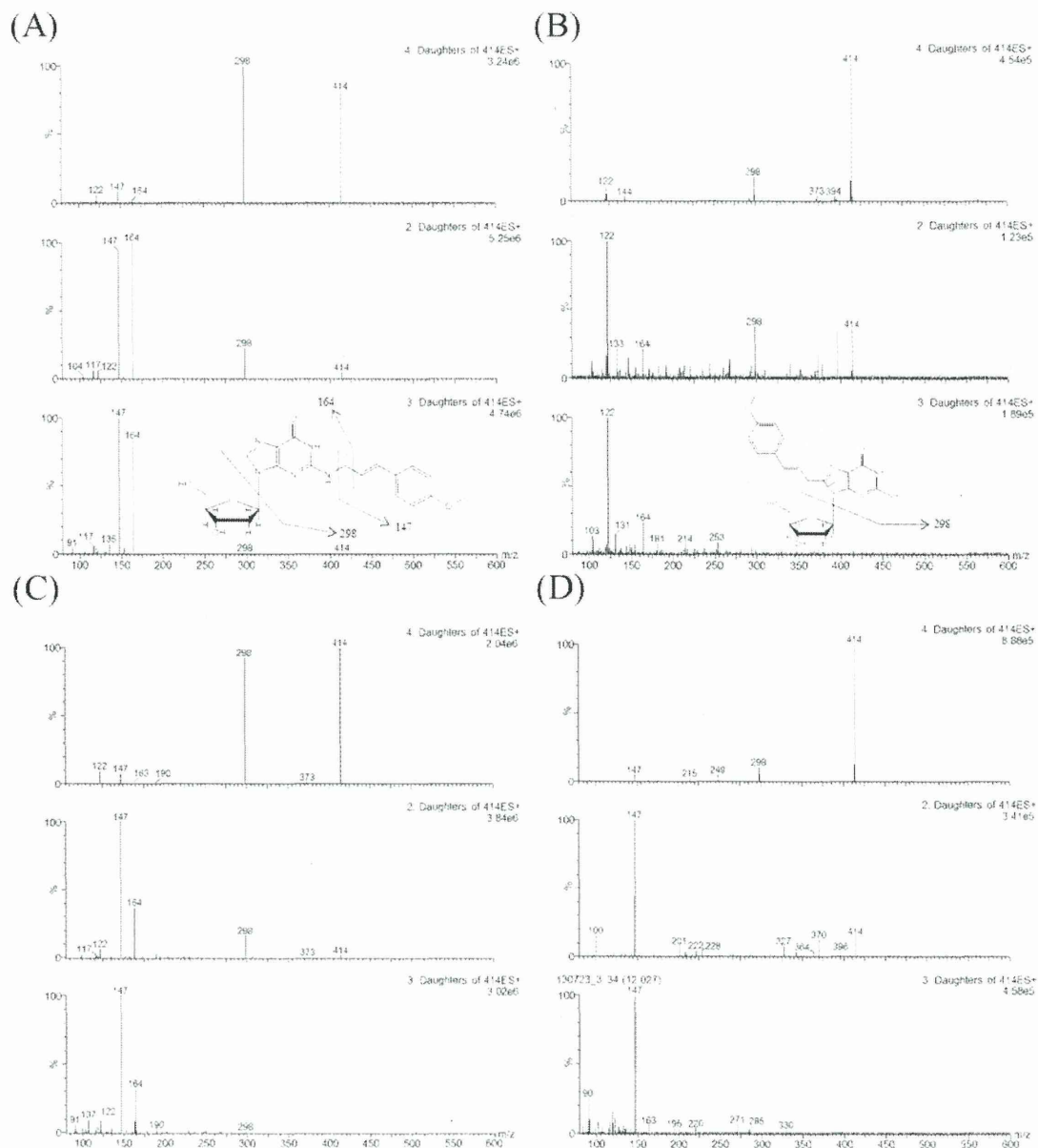
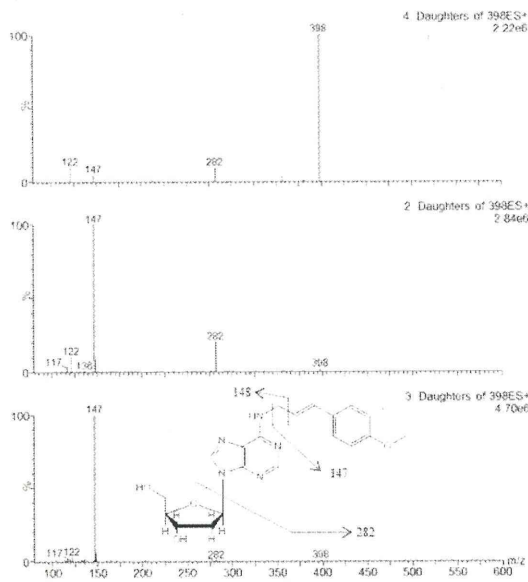


Fig. 11 Product ion spectra of putative Peak I (A) , Peak II (B), Peak V (C), and Peak VI (D) detected in the livers of ES-treated rats. The cone voltages and collision energies were set at 15 V and 5-30 eV in the positive ion mode, respectively.



(E)



(F)

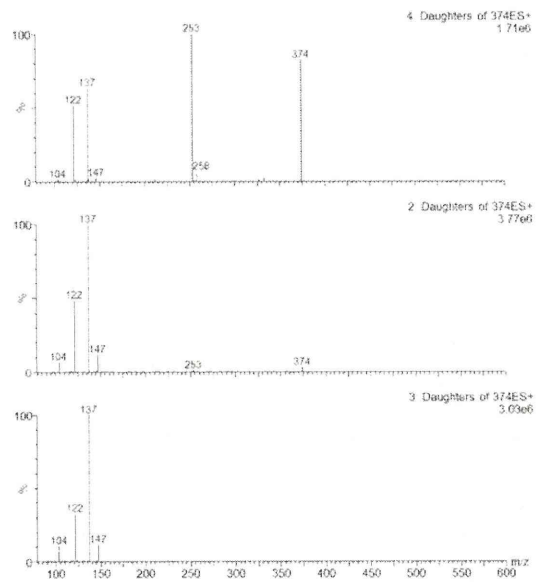
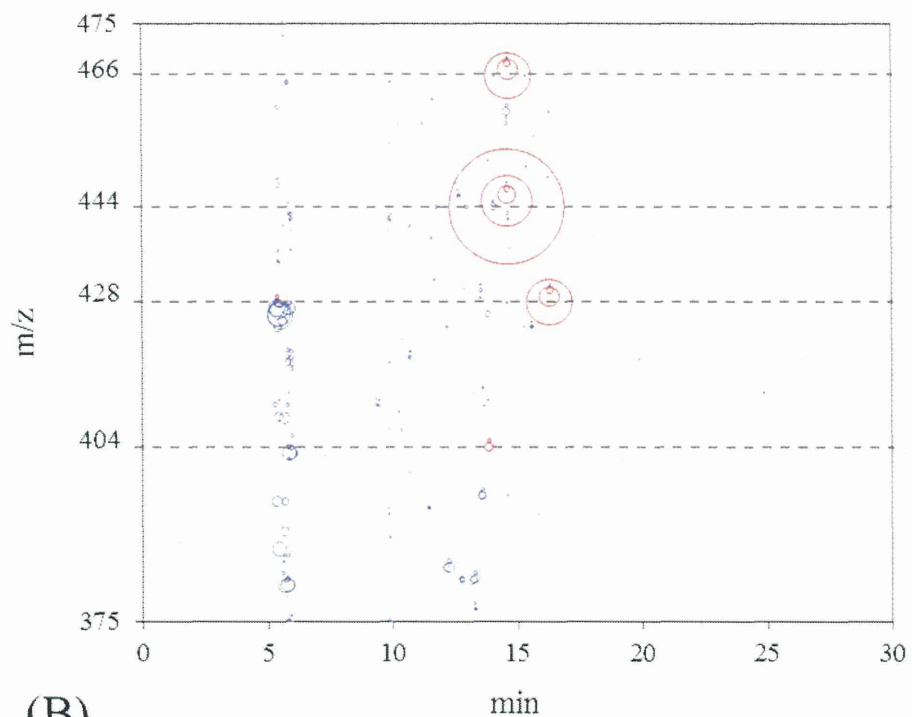


Fig. 12 DNA adductome maps of liver (A) and kidney (B) of rats treated with MEG for 4 weeks. Black and blue spots are indicating control and MEG-treated rats, respectively. Red spots are indicating putative MEG-specific DNA adducts.

(A)



(B)

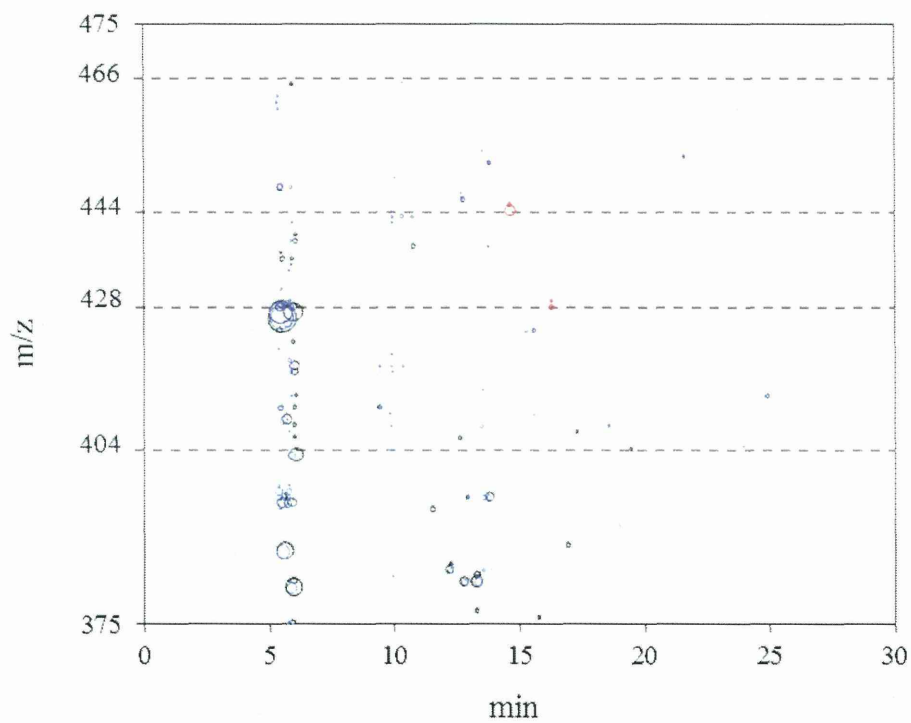


Fig. 13 Product ion spectra of putative Peak I(A) , Peak II (B), and Peak III (C) detected in the livers of MEG-treated rats. The cone voltages and collision energies were set at 15 V and 5-30 eV in the positive ion mode, respectively.

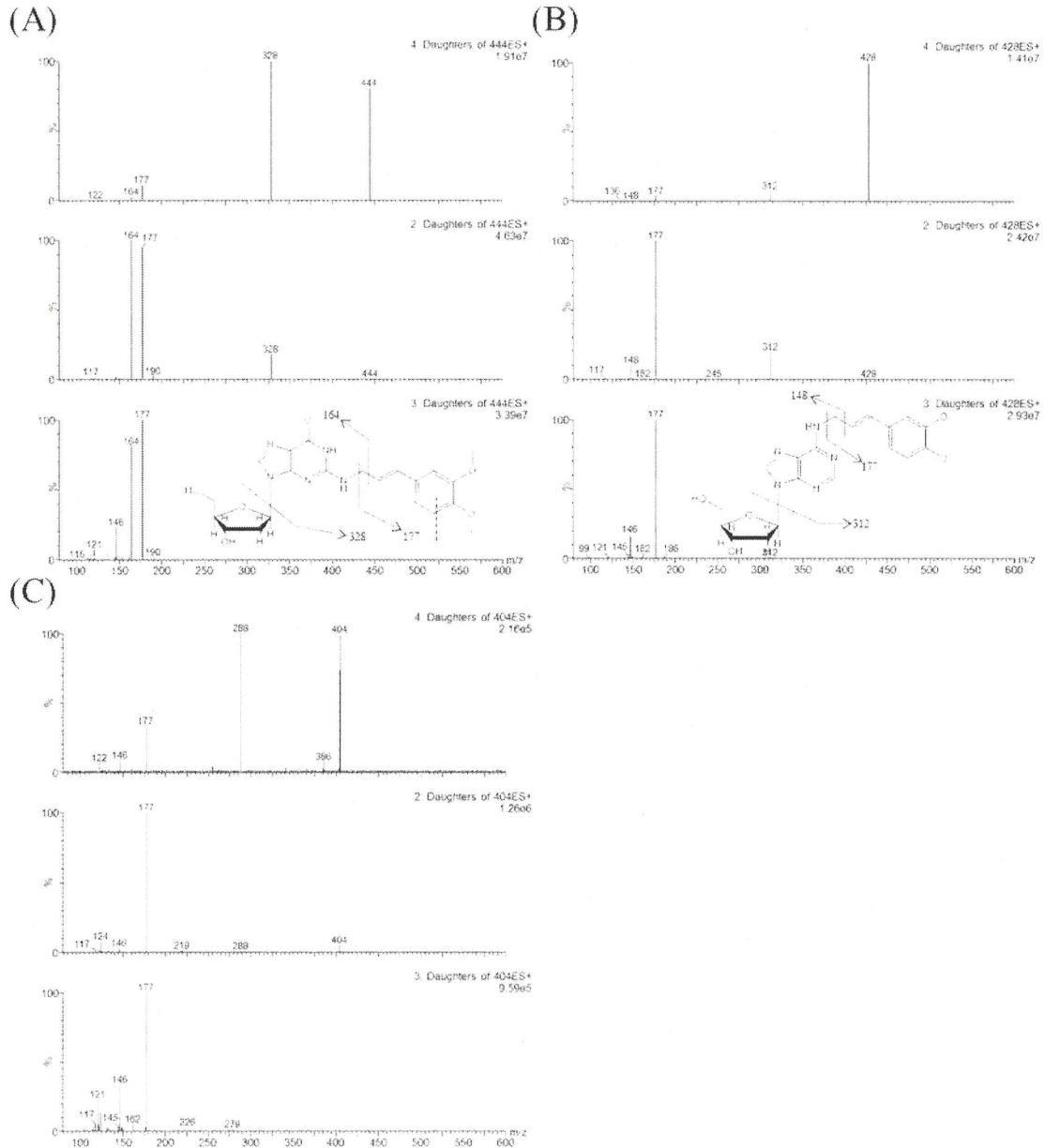
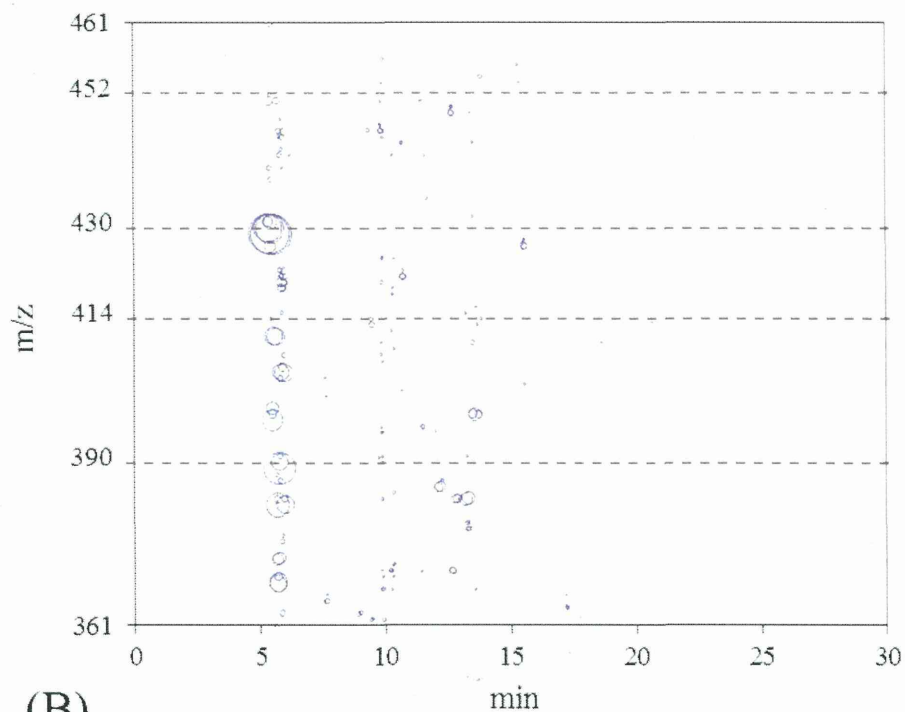


Fig. 14 DNA adductome maps of liver (A) and kidney (B) of rats treated with EG for 4 weeks. Black and blue spots are indicating control and EG-treated rats, respectively. Red spots are indicating putative EG-specific DNA adducts.

(A)



(B)

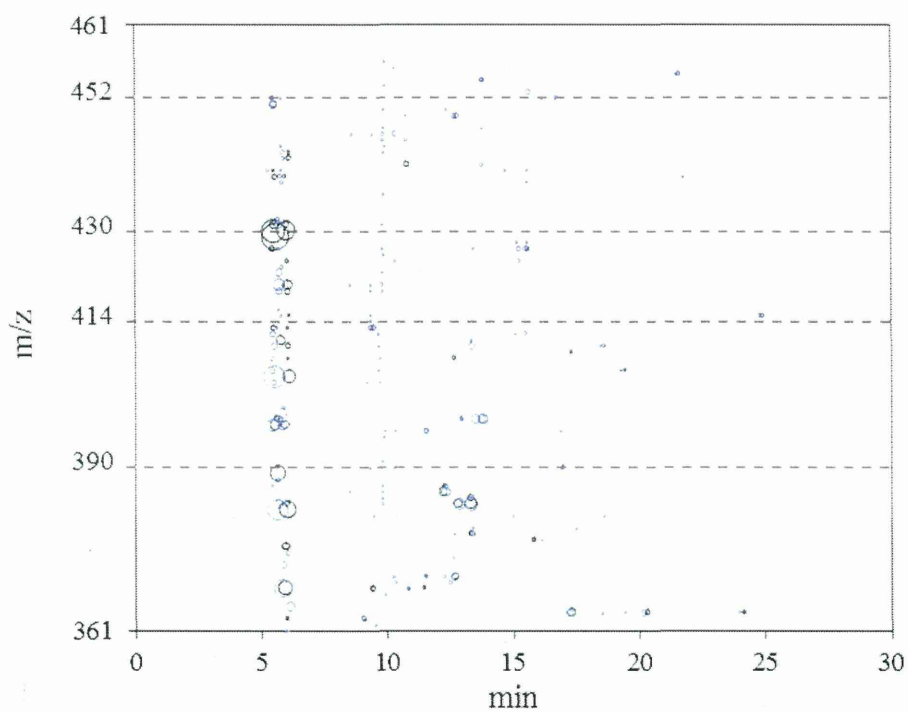


Figure 15 Mutation spectra in the livers of *gpt* delta rats treated with vehicle (A), ES (B), MEG (C), and EG (D) for 4 weeks.

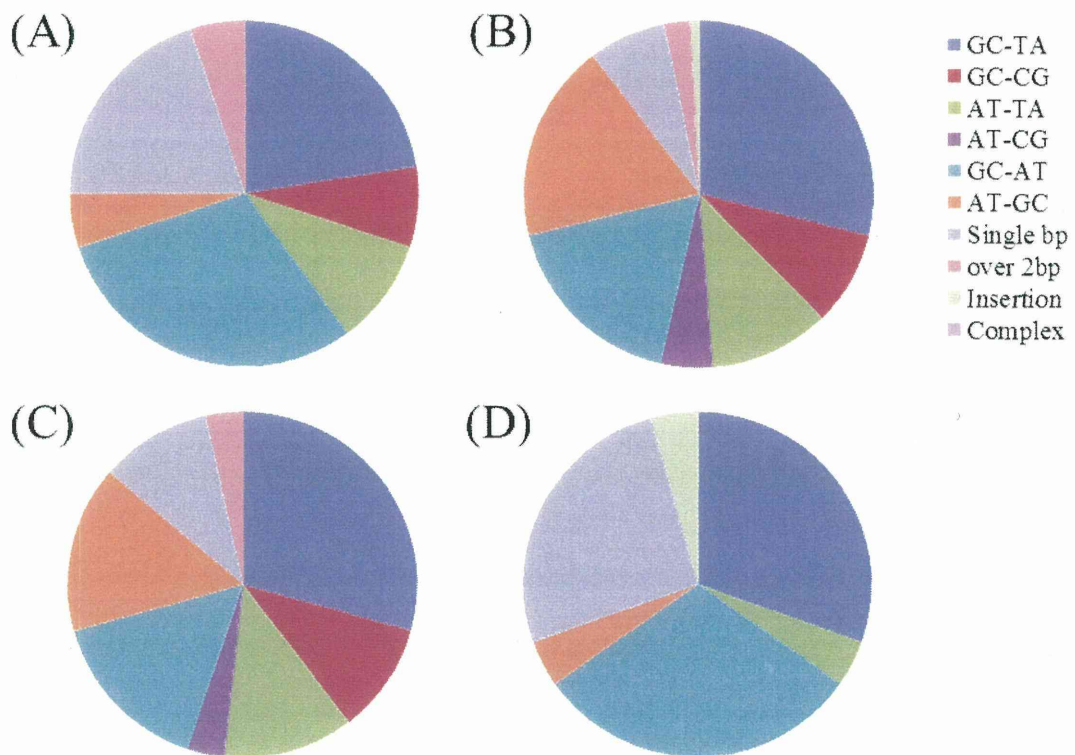


Fig. 16 MRM chromatograms of ONE induced Hε-dG (A), dA (B) and dC (C) adducts at m/z 404>288, 388>276 and 364>248 in the livers and kidneys of non-treated 10-weeks male F344 *gpt* delta rats and analytical standard

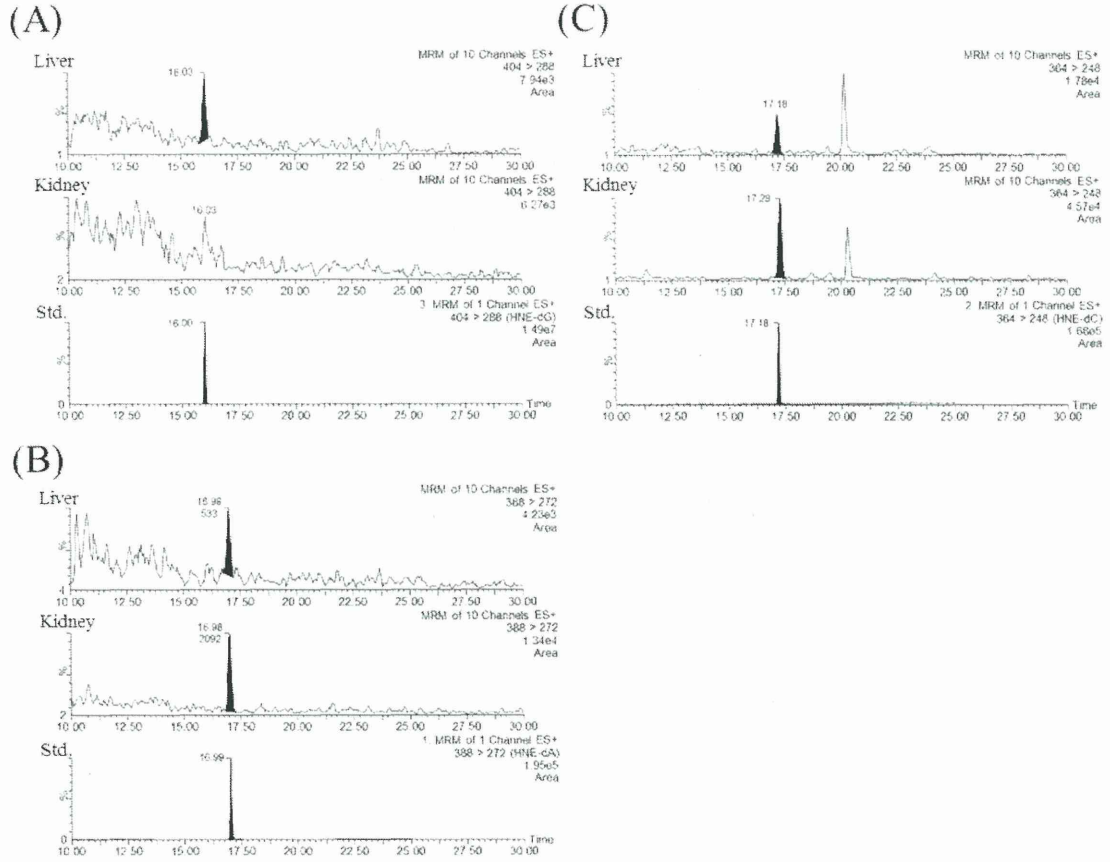


Fig. 17 Representative MRM chromatograms of He-dG (A), He-dA (C), He-dC (E) and each [¹⁵N]-labeled stable isotope (B, D, and F) in the kidneys of Alz-treated F344 *gpt* delta rats.

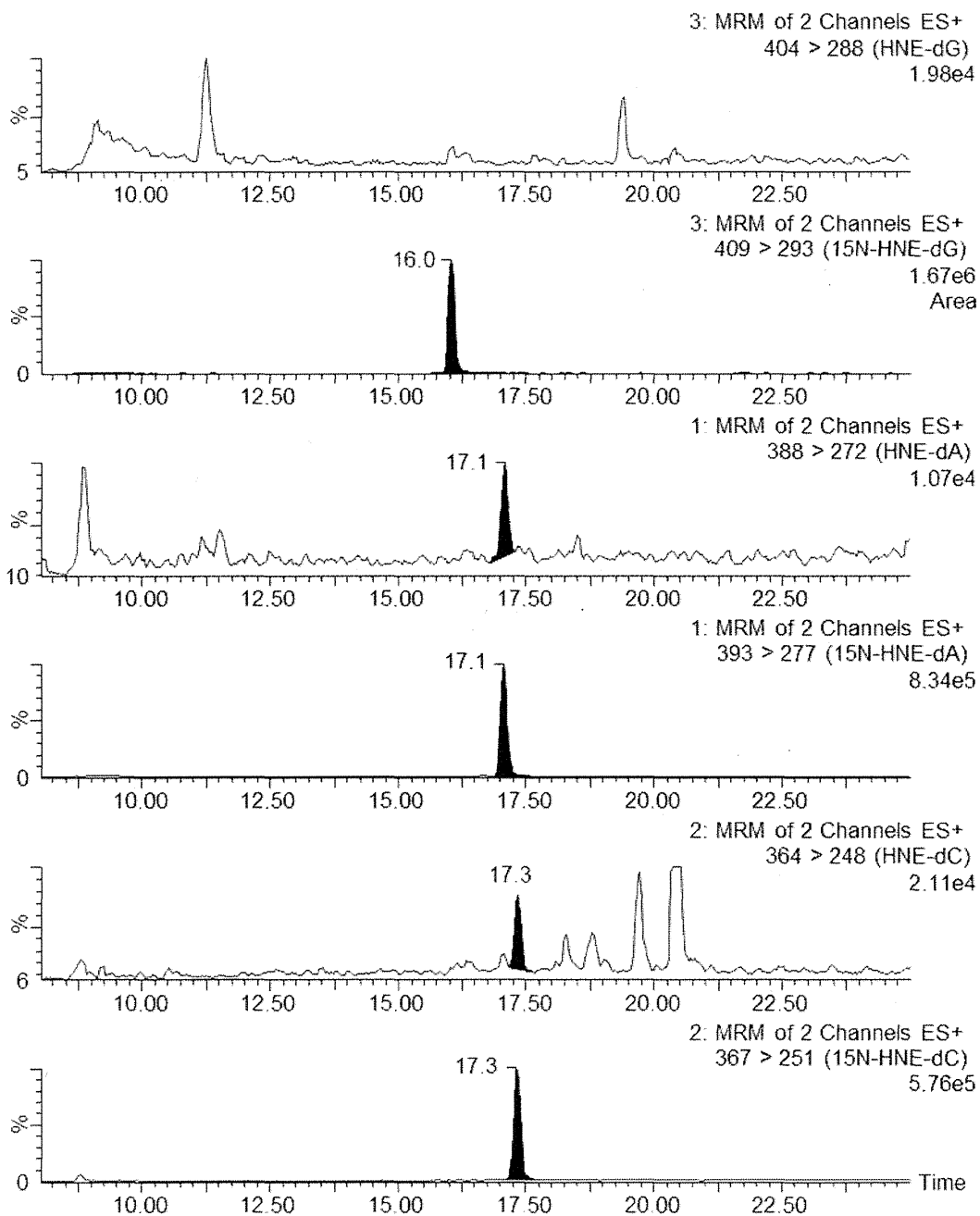


Table 1 Final body and organ weights

Item/group	Control	IQ	SFO	Alz
No. of animals	5	5	5	5
Body weight (g)	182.7 ± 15.4	204.7 ± 18.0	181.3 ± 11.7	184.2 ± 8.7
Absolute weight (g)				
Liver	7.14 ± 1.11	7.72 ± 1.05	10.24 ± 0.70**	6.63 ± 0.19
Kidney	1.33 ± 0.17	1.41 ± 0.12	1.65 ± 0.07**	1.38 ± 0.08
Relative weight (g/100g b.w.)				
Liver	3.89 ± 0.28	3.76 ± 0.19	5.65 ± 0.15**	3.60 ± 0.10
Kidney	0.73 ± 0.05	0.69 ± 0.06	0.91 ± 0.03**	0.75 ± 0.02

** : p<0.01 vs. Control group

Table 2 Summary of DNA adductome analysis

Chemicals	Organ	m/z	Retention time (min)	Peak area	Presumed adducts	Ionized type
IQ	Liver	464	12.8	2975786	IQ-C8-dG	[M+H] ⁺
		486	12.8	4149	IQ-C8-dG	[M+Na] ⁺
		480	12.8	22327	Not identified	
		448	12.5	79915	IQ-N ⁶ -dA	[M+H] ⁻
		464	11.2	19961	IQ-N ² -dG	[M+H] ⁺
	Kidney	464	12.7	624525	IQ-C8-dG	[M+H] ⁻
		448	12.4	16552	IQ-N ⁶ -dA	[M+H] ⁺
SFO	Liver	428	12.4	123041	SF-3'-C8-dG	[M+H] ⁻
		388	14.9	55236	SF-3'-N ⁴ -dC	[M+H] ⁻
		428	15.0	61049	SF-1'-N ² -dG	[M+H] ⁺
		428	15.6	7327868	SF-3'-N ² -dG	[M+H] ⁻
		450	15.6	393398	SF-3'-N ² -dG	[M+Na] ⁻
		444	15.7	18291	Not identified	
		412	17.5	2555634	SF-3'-N ⁶ -dA	[M+H] ⁻
	Kidney	428	15.7	47422	SF-3'-N ² -dG	[M+H] ⁺
		412	17.5	17966	SF-3'-N ⁶ -dA	[M+H] ⁻

Table 3 *gpt* mutant frequencies in the livers of *gpt* delta rats treated with IQ, SFO and Alz for 4 weeks

Treatment	Animal No.	Cm ^R colonies (x 10 ⁵)	6-TG ^R and Cm ^R colonies	Mutant frequency (x 10 ⁻⁵)	Mean ± SD
Control	1	9.5	2	0.21	0.76 ± 0.36
	2	9.1	5	0.55	
	3	7.7	8	1.03	
	4	9.3	6	0.65	
	5	9.7	13	1.34	
IQ	6	7.1	39	27.43	23.02 ± 3.60 **
	7	9.5	39	20.54	
	8	12.3	45	18.32	
	9	8.3	40	24.15	
	10	6.1	30	24.69	
SFO	11	6.1	10	1.63	1.88 ± 0.86
	12	5.0	7	1.41	
	13	5.2	9	1.72	
	14	3.7	12	3.21	
	15	4.9	7	1.43	
Alz	16	6.9	7	1.01	0.73 ± 0.20
	17	8.6	5	0.58	
	18	8.7	8	0.92	
	19	8.9	4	0.45	
	20	8.5	6	0.71	

** : $p < 0.01$ vs. Control group

Table 4 Spi⁻ mutant frequencies in the livers of *gpt* delta rats treated with IQ, SFO and Alz for 4 weeks

Treatment	Animal No.	Plaques within XL-1 Blue MRA ($\times 10^5$)	Plaques within WL95 (P2)	Mutant frequency ($\times 10^{-5}$)	Mean \pm SD
Control	1	15.7	5	0.32	0.43 \pm 0.13
	2	13.5	8	0.59	
	3	12.1	6	0.50	
	4	10.9	5	0.46	
	5	14.8	4	0.27	
IQ	6	6.1	47	7.68	7.41 \pm 1.42 **
	7	6.0	36	6.02	
	8	8.6	51	5.93	
	9	5.8	53	9.20	
	10	5.0	41	8.21	
SFO	11	6.7	3	0.45	0.82 \pm 0.51
	12	9.5	16	1.69	
	13	8.4	4	0.48	
	14	4.3	3	0.69	
	15	3.9	3	0.78	
Alz	16	8.1	7	0.86	0.50 \pm 0.26
	17	9.8	5	0.51	
	18	9.1	5	0.55	
	19	9.5	4	0.42	
	20	13.3	2	0.15	

** : $p < 0.01$ vs. Control group

Table 5 *gpt* mutant frequencies in the kidneys of *gpt* delta rats treated with IQ, SFO and Alz for 4 weeks

Treatment	Animal No.	Cm ^R colonies (x 10 ⁵)	6-TG ^R and Cm ^R colonies	Mutant frequency (x 10 ⁻⁵)	Mean ± SD (x 10 ⁻⁵)
Control	1	4.1	5	1.22	0.73 ± 0.41
	2	9.1	2	0.22	
	3	6.3	6	0.95	
	4	5.0	2	0.40	
	5	8.0	7	0.87	
IQ	6	6.1	29	4.74	7.04 ± 1.34**
	7	9.9	78	7.88	
	8	7.1	54	7.59	
	9	6.5	52	7.97	
	10	4.3	30	7.02	
SFO	11	1.4	1	0.74	0.68 ± 0.39
	12	3.0	1	0.33	
	13	2.4	3	1.23	
	14	4.7	3	0.64	
	15	7.5	4	0.53	
Alz	16	0.7	2	2.96	1.40 ± 0.17
	17	4.9	8	1.63	
	18	3.6	5	1.39	
	19	6.8	9	1.32	
	20	8.8	11	1.25	

***p* < 0.01 vs. Control group