Supporting Information

List of Contents

Table 1. Levels of POB-DNA adducts in rats treated with (*R*)-NNN [a]

A. Esophagus

Time (weeks)	POB-DNA adducts (fmol/mg DNA)						
	O^2-POB-dThd		7-POB-Gua		O^2-POB-Cyt		Total Adduct Levels[c]
	Mean± SD	Pecentage (%)[b]	Mean± SD	Pecentage (%)[b]	Mean ± SD	Pecentage (%)[b]	
1	110 ± 12	28%	210 ± 37	54%	70 ± 13	18%	390
2	100 ± 7	28%	200 ± 33	56%	60 ± 7	17%	360
5	100 ± 21	36%	130 ± 12	46%	50 ± 12	18%	280
10	110 ± 17	34%	150 ± 29	47%	60 ± 23	19%	320
16	100 ± 9	32%	160 ±27	52%	50 ± 14	16%	310
20	90 ± 12	35%	140 ± 41	54%	30 ± 8	12%	260

B. Liver

Time (weeks)	POB-DNA adducts (fmol/mg DNA)						
	O^2-POB-dThd		7-POB-Gua		O^2-POB-Cyt		Total Adduct Levels[c]
	Mean± SD	Pecentage (%)[b]	Mean± SD	Pecentage (%)[b]	Mean ± SD	Pecentage (%)[b]	
1	20 ± 3	57%	10 ± 4	29%	5 ± 2	14%	35
2	30 ± 3	43%	30 ± 0	42%	10 ± 4	14%	70
5	40 ± 4	50%	40 ± 0	50%	0	0%	80
10	70 ± 36	82%	10 ± 10	12%	5 ± 3	6%	85
16	70 ± 12	70%	30 ±0	30%	0	0%	100
20	40 ± 4	100%	0	0%	0	0%	40

C. Lung

Time (weeks)	POB-DNA adducts (fmol/mg DNA)						
	O^2-POB-dThd		7-POB-Gua		O^2-POB-Cyt		Total Adduct Levels[c]
	Mean± SD	Pecentage (%)[b]	Mean± SD	Pecentage (%)[b]	Mean ± SD	Pecentage (%)[b]	
1	130 ± 9	59%	60 ± 9	27%	30 ± 6	14%	220
2	210 ± 30	68%	70 ± 1	23%	30 ± 5	10%	310
5	450 ± 160	76%	110 ± 41	19%	30 ± 7	5%	590
10	660 ± 145	70%	180 ± 49	19%	100 ± 33	11%	940
16	1020 ± 804	74%	230 ±188	17%	120 ± 94	9%	1370
20	470 ± 20	72%	100 ± 11	15%	80 ± 21	12%	650

a. Each value is the mean ± S.D. of single analyses of DNA samples isolated from three rats or 3 pools of 3 rats per group at each time point.
b. The percentage was calculated by dividing the mean level of each adduct by total adduct levels
c. The value for total adduct levels is the sum of the mean levels of three POB-DNA adducts and rounded.

Table 2. Levels of POB-DNA adducts in rats treated with (*S*)-NNN [a]

A. Esophagus

Time (weeks)	POB-DNA adducts (fmol/mg DNA)						
	O^2-POB-dThd		7-POB-Gua		O^2-POB-Cyt		Total Adduct Levels[c]
	Mean ± SD	Pecentage (%)[b]	Mean ± SD	Pecentage (%)[b]	Mean ± SD	Pecentage (%)[b]	
1	340 ± 61	32%	490 ± 182	46%	240 ± 111	22%	1070
2	340 ± 52	31%	430 ± 133	39%	320 ± 47	29%	1090
5	440 ± 35	34%	550 ± 38	43%	300 ± 17	23%	1290
10	510 ± 8	37%	550 ± 88	40%	320 ± 91	23%	1380
16	460 ± 47	37%	560 ±44	44%	240 ± 14	19%	1260
20	420 ± 4	42%	360 ± 71	36%	230 ± 39	23%	1010

B. Liver

Time (weeks)	POB-DNA adducts (fmol/mg DNA)						
	O^2-POB-dThd		7-POB-Gua		O^2-POB-Cyt		Total Adduct Levels[c]
	Mean ± SD	Pecentage (%)[b]	Mean ± SD	Pecentage (%)[b]	Mean ± SD	Pecentage (%)[b]	
1	100 ± 5	59%	50 ± 2	29%	20 ± 5	12%	170
2	170 ± 23	50%	140 ± 15	41%	30 ± 9	9%	340
5	240 ± 43	62%	120 ± 22	31%	30 ±8	8%	390
10	310 ± 28	78%	70 ± 14	18%	20 ± 5	5%	400
16	370 ± 111	74%	110 ±30	22%	20 ±0	4%	500
20	300 ± 32	73%	70 ±8	17%	40 ±13	10%	410

C. Lung

Time (weeks)	POB-DNA adducts (fmol/mg DNA)						
	O^2-POB-dThd		7-POB-Gua		O^2-POB-Cyt		Total Adduct Levels[c]
	Mean ± SD	Pecentage (%)[b]	Mean ± SD	Pecentage (%)[b]	Mean ± SD	Pecentage (%)[b]	
1	50 ± 5	63%	20 ±6	25%	10 ± 3	13%	80
2	80 ± 7	67%	30 ± 8	25%	10 ± 3	8%	120
5	160 ± 12	76%	40 ± 2	19%	10 ± 2	5%	210
10	260 ± 28	70%	70 ± 14	19%	40 ± 7	11%	370
16	290 ± 3	76%	60 ±8	16%	30 ± 3	8%	380
20	230 ± 24	74%	50 ± 6	16%	30 ± 6	10%	310

a. Each value is the mean ± S.D. of single analyses of DNA samples isolated from three rats or 3 pools of 3 rats per group at each time point.
b. The percentage was calculated by dividing the mean level of each adduct by total adduct levels
c. The value for total adduct levels is the sum of the mean levels of three POB-DNA adducts and rounded.

Table 3. Levels of POB-DNA adducts in rats treated for 20 weeks with (*R*)-NNN or (*S*)-NNN[a]

Tissue	Group	O^2-POB-dThd (fmol/µmol dThd)[b]	O^2-POB-Cyt (fmol/µmol dCyd)[b]	7-POB-Gua (fmol/µmol dGuo)[b]
Esophagus	(*R*)-NNN	110 ± 16	50 ± 8	210 ± 62
	(*S*)-NNN	560 ± 4	410 ± 64	550 ± 108
Liver	(*R*)-NNN	50 ± 7	0	0
	(*S*)-NNN	470 ± 40	80 ± 21	110 ± 13
Lung	(*R*)-NNN	600 ± 26	150 ± 40	150 ± 17
	(*S*)-NNN	300 ± 32	60 ± 11	80 ± 9

a. Each value is the mean ± S.D. of single analyses of DNA samples isolated from three rats or 3 pools of 3 rats per group at each time point.

b. Levels of each POB-DNA adduct were expressed as fmol per appropriate µmol nucleoside. Contents of dGuo, dThd and dCyd were determined by HPLC.

Table 4. Statistical comparison of levels of each individual POB-DNA adduct [a]

A. Esophagus

Time (weeks)	(*R*)-NNN			(*S*)-NNN		
	11[b] *vs* **14**[b]	**11** *vs* **15**[b]	**14** *vs* **15**	**11** *vs* **14**	**11** *vs* **15**	**14** *vs* **15**
1	*P* <0.01	*P* <0.01	*P* <0.01	NS	NS	*P* <0.01
2	*P* <0.01	*P* <0.01	*P* <0.01	NS	NS	NS
5	NS[c]	NS	NS	NS	*P* <0.01	*P* <0.01
10	NS	NS	NS	NS	NS	NS
16	NS	NS	*P* <0.01	NS	*P* <0.01	*P* <0.01
20	NS	*P* <0.01	*P* <0.01	NS	*P* <0.01	NS

B. Liver

Time (weeks)	(*R*)-NNN			(*S*)-NNN		
	11 *vs* **14**	**11** *vs* **15**	**14** *vs* **15**	**11** *vs* **14**	**11** *vs* **15**	**14** *vs* **15**
1	NS	*P* <0.01	NS	*P* <0.01	*P* <0.01	*P* <0.01
2	NS	NS	NS	NS	*P* <0.01	*P* <0.01
5	NA[d]	NA	NA	*P* <0.01	*P* <0.01	*P* <0.01
10	*P* <0.01	*P* <0.01	NS	*P* <0.01	*P* <0.01	*P* <0.01
16	NA	NA	NA	*P* <0.01	*P* <0.01	*P* <0.01
20	NA	NA	NA	*P* <0.01	*P* <0.01	NS

C. Lung

Time (weeks)	(*R*)-NNN			(*S*)-NNN		
	11 *vs* **14**	**11** *vs* **15**	**14** *vs* **15**	**11** *vs* **14**	**11** *vs* **15**	**14** *vs* **15**
1	*P* <0.01	*P* <0.01	*P* <0.01	*P* <0.01	*P* <0.01	*P* <0.01
2	*P* <0.01	*P* <0.01	*P* <0.01	*P* <0.01	*P* <0.01	*P* <0.01
5	*P* <0.01	*P* <0.01	*P* <0.01	*P* <0.01	*P* <0.01	*P* <0.01
10	*P* <0.01	*P* <0.01	*P* <0.01	*P* <0.01	*P* <0.01	*P* <0.01
16	*P* <0.01	*P* <0.01	*P* <0.01	*P* <0.01	*P* <0.01	*P* <0.01
20	*P* <0.01	*P* <0.01	NS	*P* <0.01	*P* <0.01	*P* <0.01

a. A repeated measures analysis of variance was used to compare each adduct within each group at each time point.
b. Compound **11**: O^2 -POB-dThd; **14**:7-POB-Gua; **15**: O^2 -POB-Cyt.
c. NS: no significant difference ($P > 0.01$)
d. NA: not available due to levels of O^2 -POB-Cyt below the limit of detection of HPLC-ESI-MS/MS analysis