

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

A. Esophagus

Time (weeks)	POB-DNA adducts (fmol/mg DNA)						Total Adduct Levels ^c
	<i>O</i> ² -POB-dThd		7-POB-Gua		<i>O</i> ² -POB-Cyt		
	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^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)						Total Adduct Levels ^c
	<i>O</i> ² -POB-dThd		7-POB-Gua		<i>O</i> ² -POB-Cyt		
	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^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)						Total Adduct Levels ^c
	<i>O</i> ² -POB-dThd		7-POB-Gua		<i>O</i> ² -POB-Cyt		
	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^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)						Total Adduct Levels ^c
	<i>o</i> ² -POB-dThd		7-POB-Gua		<i>o</i> ² -POB-Cyt		
	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^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)						Total Adduct Levels ^c
	<i>o</i> ² -POB-dThd		7-POB-Gua		<i>o</i> ² -POB-Cyt		
	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^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)						Total Adduct Levels ^c
	<i>o</i> ² -POB-dThd		7-POB-Gua		<i>o</i> ² -POB-Cyt		
	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^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	(<i>R</i>)-NNN	110 ± 16	50 ± 8	210 ± 62
	(<i>S</i>)-NNN	560 ± 4	410 ± 64	550 ± 108
Liver	(<i>R</i>)-NNN	50 ± 7	0	0
	(<i>S</i>)-NNN	470 ± 40	80 ± 21	110 ± 13
Lung	(<i>R</i>)-NNN	600 ± 26	150 ± 40	150 ± 17
	(<i>S</i>)-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	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	NS	NS	<i>P</i> <0.01
2	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	NS	NS	NS
5	NS ^c	NS	NS	NS	<i>P</i> <0.01	<i>P</i> <0.01
10	NS	NS	NS	NS	NS	NS
16	NS	NS	<i>P</i> <0.01	NS	<i>P</i> <0.01	<i>P</i> <0.01
20	NS	<i>P</i> <0.01	<i>P</i> <0.01	NS	<i>P</i> <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	<i>P</i> <0.01	NS	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01
2	NS	NS	NS	NS	<i>P</i> <0.01	<i>P</i> <0.01
5	NA ^d	NA	NA	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01
10	<i>P</i> <0.01	<i>P</i> <0.01	NS	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01
16	NA	NA	NA	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01
20	NA	NA	NA	<i>P</i> <0.01	<i>P</i> <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	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01
2	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01
5	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01
10	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01
16	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01
20	<i>P</i> <0.01	<i>P</i> <0.01	NS	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <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