

Table 1. Levels of POB-DNA adducts in liver DNA ^a

A. NNK

Time (weeks)	POB-DNA adducts (fmol/mg DNA)						Total Adduct Levels ^c
	O ² -POB-dThd		7-POB-Gua		O ² -POB-Cyt		
	Mean± SD	Percentage (%) ^b	Mean± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	
1	650 ± 121	49.6%	490 ± 104	37.4%	170 ± 43	13.0%	1310
2	1230 ± 272	54.7%	880 ± 182	39.1%	140 ± 25	6.2%	2250
5	2190 ± 174	62.9%	1050 ± 90	30.2%	240 ± 17	6.9%	3480
10	3740 ± 1169	64.7%	1460 ± 625	25.3%	580 ± 214	10.0%	5780
16	3540 ± 643	70.0%	1170 ± 86	23.1%	350 ± 152	6.9%	5060
20	2680 ± 643	68.7%	730 ± 225	18.7%	490 ± 146	12.6%	3900

B. (R)-NNAL

Time (weeks)	POB-DNA adducts (fmol/mg DNA)						Total Adduct Levels ^c
	O ² -POB-dThd		7-POB-Gua		O ² -POB-Cyt		
	Mean± SD	Percentage (%) ^b	Mean± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	
1	70 ± 15	63.6%	40 ± 12	36.4%	0	0.0%	110
2	90 ± 4	60.0%	60 ± 12	40.0%	0	0.0%	150
5	140 ± 11	77.8%	40 ± 11	22.2%	20 ± 9	0.0%	180
10	270 ± 101	79.4%	50 ± 20	14.7%	0	5.9%	340
16	260 ± 92	83.9%	50 ± 31	16.1%	0	0.0%	310
20	200 ± 47	83.3%	40 ± 5	16.7%	0	0.0%	240

C. (S)-NNAL

Time (weeks)	POB-DNA adducts (fmol/mg DNA)						Total Adduct Levels ^c
	O ² -POB-dThd		7-POB-Gua		O ² -POB-Cyt		
	Mean± SD	Percentage (%) ^b	Mean± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	
1	990 ± 361	52.4%	660 ± 231	34.9%	240 ± 95	12.7%	1890
2	1100 ± 121	61.1%	590 ± 106	32.8%	110 ± 20	6.1%	1800
5	1910 ± 378	68.5%	680 ± 94	24.4%	200 ± 44	7.2%	2790
10	2700 ± 301	74.2%	690 ± 68	19.0%	250 ± 17	6.9%	3640
16	2530 ± 360	68.8%	920 ± 58	25.0%	230 ± 38	6.3%	3680
20	1910 ± 243	69.7%	470 ± 86	17.2%	360 ± 47	13.1%	2740

- a. Each value is the mean ± S.D. of single analyses of DNA samples isolated from three 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 lung DNA ^a

A. NNK

Time (weeks)	POB-DNA adducts (fmol/mg DNA)								
	O ² -POB-dThd		7-POB-Gua		O ² -POB-Cyt		O ⁶ -POB-dGuo		Total Adduct Levels ^c
	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	
1	1080 ± 99	51.1%	750 ± 95	35.5%	240 ± 23	11.3%	45 ± 7	2.1%	2120
2	2020 ± 150	57.7%	1180 ± 131	33.7%	250 ± 18	7.1%	50 ± 5	1.4%	3500
5	3890 ± 648	68.3%	1360 ± 214	23.9%	400 ± 87	7.0%	46 ± 13	0.8%	5700
10	8260 ± 2731	73.4%	2220 ± 864	19.7%	730 ± 211	6.5%	44 ± 14	0.4%	11250
16	6720 ± 606	72.5%	1700 ± 175	18.4%	810 ± 152	8.7%	34 ± 17	0.4%	9260
20	5070 ± 1057	71.5%	1060 ± 169	15.0%	940 ± 175	13.3%	20 ± 5	0.3%	7090

B. (R)-NNAL

Time (weeks)	POB-DNA adducts (fmol/mg DNA)								
	O ² -POB-dThd		7-POB-Gua		O ² -POB-Cyt		O ⁶ -POB-dGuo		Total Adduct Levels ^c
	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	
1	100 ± 8	51.8%	60 ± 4	31.1%	30 ± 11	15.5%	3 ± 0	1.6%	190
2	160 ± 13	56.7%	100 ± 10	35.5%	20 ± 2	7.1%	2 ± 1	0.7%	280
5	280 ± 18	67.8%	100 ± 3	24.2%	30 ± 5	7.3%	3 ± 0	0.7%	410
10	790 ± 38	75.7%	200 ± 17	19.2%	50 ± 8	4.8%	3 ± 0	0.3%	1040
16	630 ± 35	78.8%	130 ± 11	16.3%	40 ± 12	5.0%	0	0.0%	800
20	480 ± 18	75.0%	100 ± 11	15.6%	60 ± 10	9.4%	0	0.0%	640

C. (S)-NNAL

Time (weeks)	POB-DNA adducts (fmol/mg DNA)								
	O ² -POB-dThd		7-POB-Gua		O ² -POB-Cyt		O ⁶ -POB-dGuo		Total Adduct Levels ^c
	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	Mean ± SD	Percentage (%) ^b	
1	1410 ± 304	50.2%	960 ± 222	34.2%	390 ± 102	13.9%	50 ± 13	1.8%	2810
2	1980 ± 126	58.2%	1150 ± 64	33.8%	230 ± 21	6.8%	40 ± 5	1.2%	3400
5	3340 ± 141	70.5%	1080 ± 39	22.8%	290 ± 11	6.1%	30 ± 2	0.6%	4740
10	5120 ± 608	76.1%	1160 ± 193	17.2%	420 ± 58	6.2%	30 ± 4	0.4%	6730
16	6400 ± 355	73.3%	1520 ± 94	17.4%	790 ± 87	9.0%	20 ± 6	0.2%	8730
20	4980 ± 65	69.8%	1110 ± 75	15.6%	1020 ± 73	14.3%	20 ± 2	0.3%	7130

- a. Each value is the mean ± S.D. of single analyses of DNA samples isolated from three 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 four POB-DNA adducts and rounded.

Table 3. Levels of POB-DNA adducts in rats treated with NNK, (R)-NNAL or (S)-NNAL for 20 weeks ^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
NNK	liver	4180 ± 967	830 ± 208	1100 ± 341
	lung	6450 ± 1351	1820 ± 336	1610 ± 256
(R)-NNAL	liver	310 ± 74	0	60 ± 8
	lung	550 ± 88	90 ± 29	150 ± 16
(S)-NNAL	liver	2730 ± 615	660 ± 63	720 ± 130
	lung	6420 ± 82	1990 ± 135	1680 ± 113

a. Each value is the mean ± S.D. of single analyses of DNA samples isolated from three 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 in liver and lung of rats treated with NNK, (R)-NNAL, or (S)-NNAL ^a

A. NNK

Time (weeks)	Liver			Lung					
	13^b vs 16^b	13 vs 17^b	16 vs 17	13 vs 16	13 vs 17	16 vs 17	12^b vs 13	12 vs 16	12 vs 17
1	NS ^c	<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	<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	<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	<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	<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	NS	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01

B. (R)-NNAL

Time (weeks)	Liver	Lung					
	13 vs 16	13 vs 16	13 vs 17	16 vs 17	12 vs 13	12 vs 16	12 vs 17
1	NS	<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	NS	<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	<i>P</i> <0.01
10	NS	<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	NS	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	NA ^d	NA	NA
20	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	<i>P</i> <0.01	NA	NA	NA

C. (S)-NNAL

Time (weeks)	Liver			Lung					
	13 vs 16	13 vs 17	16 vs 17	13 vs 16	13 vs 17	16 vs 17	12 vs 13	12 vs 16	12 vs 17
1	NS	<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	<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	<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	<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	<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	<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	<i>P</i> <0.01	<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 **12**: *O*⁶-POB-dGuo; **13**: *O*²-POB-dThd; **16**: 7-POB-Gua; **17**: *O*²-POB-Cyt.

c. NS: no significant difference (*P* > 0.01)

d. NA: not available due to level of *O*⁶-POB-dGuo below the limit of detection of HPLC-ESI-MS/MS analysis