

ADME NTP Study S0209 Nalidixic acid

The contract laboratory used the abbreviation NA for the test article.

Sex/Species: adult male F344 rats and B6C3F1 mice.

Vehicles: oral, corn oil.

CASRN 389-08-2

Radiolabeled with carbon-14 in the 3-position; Nalidixic acid, [3-¹⁴C]-

Studies Performed:

- Single 20, 200, or 500 mg NA/kg oral gavage dose in male and female mice with sacrifice 72 hours postdose.
- Single 20, 200, or 500 mg NA/kg oral gavage dose in male and female rats with sacrifice 72 hours postdose.

No radioactivity was detected in the expired air.

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Table 1: Urinary excretion of ¹⁴C radioactivity by male mice after oral administration of [¹⁴C]NA

Time (hr)	20 mg/kg^a	200 mg/kg^b	500 mg/kg^b
<i>Mean ± SD dose excreted (%)</i>			
0-4	0.0 ± 0.0	10.6 ± 3.8	8.7 ± 3.3
4-8	5.6 ± 7.3	3.0 ± 3.4	3.5 ± 3.7
8-24	18.3 ± 6.3	24.9 ± 5.5	24.0 ± 4.9
24-48	6.1 ± 5.1	5.0 ± 2.2	3.1 ± 1.3
48-72	5.4 ± 6.0	2.2 ± 1.6	0.8 ± 0.1
<i>Mean ± SD dose excreted (cumulative %)</i>			
0-4	0.0 ± 0.0	10.6 ± 3.8	8.7 ± 3.3
0-8	5.6 ± 7.3	13.7 ± 5.7	12.2 ± 4.1
0-24	23.9 ± 10.1	38.6 ± 10.6	36.2 ± 6.6
0-48	30.0 ± 8.7	43.6 ± 8.6	39.3 ± 6.4
0-72	35.4 ± 2.9	45.7 ± 7.2	40.1 ± 6.4

^aData from three mice.

^bData from four mice.

Table 2: Urinary excretion of ¹⁴C radioactivity by female mice after oral administration of [¹⁴C]NA

Time (hr)	20 mg/kg ^a	200 mg/kg ^b	500 mg/kg ^b
	<i>Mean ± SD dose excreted (%)</i>		
0-4	7.7 ± 7.2	7.7 ± 3.7	3.3 ± 2.9
4-8	9.9 ± 2.5	2.6 ± 1.8	4.0 ± 4.1
8-24	18.1 ± 4.9	20.2 ± 2.7	18.1 ± 8.7
24-48	6.2 ± 5.7	6.3 ± 3.6	9.1 ± 10.0
48-72	4.5 ± 4.3	3.8 ± 1.5	1.5 ± 0.4
	<i>Mean ± SD dose excreted (cumulative %)</i>		
0-4	7.7 ± 7.2	7.7 ± 3.7	3.3 ± 2.9
0-8	17.6 ± 7.9	10.3 ± 2.5	7.3 ± 4.7
0-24	35.7 ± 10.4	30.5 ± 4.0	25.4 ± 12.9
0-48	41.9 ± 5.4	36.9 ± 1.3	34.5 ± 4.0
0-72	46.3 ± 3.5	40.6 ± 0.7	35.9 ± 4.0

^aData from five mice.

^bData from four mice.

Table 3: Urinary excretion of ¹⁴C radioactivity by male rats after oral administration of [¹⁴C]NA

Time (hr)	20 mg/kg^a	200 mg/kg^b	500 mg/kg^b
<i>Mean ± SD dose excreted (%)</i>			
0-4	3.4 ± 5.1	6.4 ± 2.0	3.7 ± 1.3
4-8	9.3 ± 10.9	12.8 ± 4.9	2.3 ± 1.9
8-24	61.3 ± 17.7	41.2 ± 3.9	20.3 ± 1.5
24-48	4.2 ± 2.9	12.6 ± 2.0	30.2 ± 3.7
48-72	0.8 ± 0.7	1.4 ± 0.4	4.6 ± 1.1
<i>Mean ± SD dose excreted (cumulative %)</i>			
0-4	3.4 ± 5.1	6.4 ± 2.0	3.7 ± 1.3
0-8	12.7 ± 14.8	19.2 ± 3.1	6.0 ± 1.5
0-24	74.1 ± 9.7	60.4 ± 6.9	26.3 ± 2.6
0-48	78.3 ± 7.8	73.0 ± 5.0	56.5 ± 5.9
0-72	79.1 ± 7.8	74.4 ± 4.6	61.2 ± 5.1

^aData from four rats.

^bData from three rats.

Table 4: Urinary excretion of ¹⁴C radioactivity by female rats after oral administration of [¹⁴C]NA

Time (hr)	20 mg/kg	200 mg/kg	500 mg/kg
	<i>Mean ± SD dose excreted (%)^a</i>		
0-4	9.2 ± 10.8	5.4 ± 1.5	1.8 ± 1.0
4-8	18.6 ± 21.6	9.1 ± 5.9	2.6 ± 0.8
8-24	43.5 ± 15.7	43.9 ± 9.9	12.1 ± 5.4
24-48	2.0 ± 0.5	13.1 ± 8.5	30.1 ± 4.5
48-72	0.6 ± 0.2	0.7 ± 0.6	10.7 ± 6.6
	<i>Mean ± SD dose excreted (cumulative %)</i>		
0-4	9.2 ± 10.8	5.4 ± 1.5	1.8 ± 1.0
0-8	27.8 ± 11.3	14.5 ± 5.2	4.3 ± 0.9
0-24	71.2 ± 4.8	58.4 ± 14.7	16.4 ± 5.8
0-48	73.2 ± 4.8	71.5 ± 8.2	46.5 ± 8.3
0-72	73.8 ± 4.7	72.1 ± 8.4	57.2 ± 7.6

^aData from four rats.

Table 5: Fecal excretion of ¹⁴C radioactivity by male mice after oral administration of [¹⁴C]NA

Time (hr)	20 mg/kg^a	200 mg/kg^b	500 mg/kg^b
<i>Mean ± SD dose excreted (%)</i>			
0-4	0.0 ± 0.1	0.6 ± 0.5	1.2 ± 1.6
4-8	0.0 ± 0.1	1.2 ± 0.8	1.0 ± 1.2
8-24	23.2 ± 7.9	19.4 ± 3.2	26.9 ± 4.0
24-48	10.8 ± 10.4	0.5 ± 0.3	2.3 ± 1.7
48-72	2.6 ± 2.7	8.2 ± 5.3	2.2 ± 1.2
<i>Mean ± SD dose excreted (cumulative %)</i>			
0-4	0.0 ± 0.1	0.6 ± 0.5	1.2 ± 1.6
0-8	0.1 ± 0.1	1.8 ± 1.2	2.2 ± 1.6
0-24	23.3 ± 8.0	21.2 ± 2.9	29.1 ± 5.1
0-48	34.1 ± 4.2	21.7 ± 2.9	31.4 ± 3.5
0-72	36.7 ± 6.2	29.9 ± 5.7	33.6 ± 3.6

^aData from four mice.

^bData from three mice.

Table 6: Fecal excretion of ^{14}C radioactivity by female mice after oral administration of ^{14}C NA

Time (hr)	20 mg/kg ^a	200 mg/kg ^b	500 mg/kg ^b
<i>Mean ± SD dose excreted (%)</i>			
0-4	0.5 ± 0.5	0.9 ± 0.4	0.2 ± 0.2
4-8	3.5 ± 4.7	5.6 ± 3.1	2.3 ± 1.3
8-24	18.6 ± 8.1	20.7 ± 4.7	17.9 ± 11.8
24-48	5.1 ± 5.5	0.5 ± 0.2	2.0 ± 0.7
48-72	3.0 ± 3.9	6.8 ± 5.1	11.0 ± 15.0
<i>Mean ± SD dose excreted (cumulative %)</i>			
0-4	0.5 ± 0.5	0.9 ± 0.4	0.2 ± 0.2
0-8	4.1 ± 4.7	6.4 ± 3.2	2.5 ± 1.3
0-24	22.7 ± 6.0	27.2 ± 7.4	20.4 ± 12.9
0-48	27.8 ± 1.4	27.7 ± 7.4	22.4 ± 12.6
0-72	30.8 ± 4.5	34.5 ± 5.7	33.4 ± 3.6

^aData from five mice.

^bData from four mice.

Table 7: Fecal excretion of ¹⁴C radioactivity by male rats after oral administration of [¹⁴C]NA

Time (hr)	20 mg/kg ^a	200 mg/kg ^b	500 mg/kg ^b
<i>Mean ± SD dose excreted (%)</i>			
0-4	0.1 ± 0.1	0.2 ± 0.3	0.5 ± 0.4
4-8	0.2 ± 0.3	0.9 ± 0.5	0.0 ± 0.1
8-24	7.8 ± 1.8	3.0 ± 1.4	1.4 ± 1.1
24-48	4.9 ± 1.7	13.1 ± 4.1	4.1 ± 5.2
48-72	0.4 ± 0.1	1.7 ± 1.0	14.7 ± 4.9
<i>Mean ± SD dose excreted (cumulative %)</i>			
0-4	0.1 ± 0.1	0.2 ± 0.3	0.5 ± 0.4
0-8	0.2 ± 0.3	1.1 ± 0.8	0.6 ± 0.3
0-24	8.0 ± 2.0	4.1 ± 2.1	2.0 ± 1.4
0-48	13.0 ± 2.3	17.1 ± 3.7	6.1 ± 4.6
0-72	13.4 ± 2.3	18.8 ± 4.4	20.8 ± 4.5

^aData from four rats.^bData from three rats.

Table 8: Fecal excretion of ¹⁴C radioactivity by female rats after oral administration of [¹⁴C]NA

Time (hr)	20 mg/kg	200 mg/kg	500 mg/kg
<i>Mean ± SD dose excreted (%)^a</i>			
0-4	0.0 ± 0.0	0.2 ± 0.2	0.2 ± 0.1
4-8	0.2 ± 0.3	0.3 ± 0.3	0.7 ± 0.5
8-24	7.5 ± 2.5	1.9 ± 0.7	1.7 ± 1.9
24-48	3.9 ± 1.5	14.7 ± 6.0	5.6 ± 5.3
48-72	0.2 ± 0.1	2.1 ± 2.9	23.3 ± 2.4
<i>Mean ± SD dose excreted (cumulative %)</i>			
0-4	0.0 ± 0.0	0.2 ± 0.2	0.2 ± 0.1
0-8	0.2 ± 0.3	0.5 ± 0.4	0.9 ± 0.5
0-24	7.7 ± 2.4	2.3 ± 0.5	2.6 ± 1.8
0-48	11.6 ± 1.4	17.0 ± 6.1	8.1 ± 6.1
0-72	11.8 ± 1.5	19.1 ± 3.7	31.4 ± 7.4

^aData from four rats.

Table 9: Concentration of [¹⁴C]NA equivalents in tissues of male mice at 72 hr after oral administration of [¹⁴C]NA

Tissue	Mean ± SD concentration (nmol/g)		
	20 mg/kg ^a	200 mg/kg ^b	500 mg/kg ^b
Plasma	0.07 ± 0.01	0.83 ± 0.59	1.44 ± 0.54
Blood cells	0.00 ± 0.00	0.00 ± 0.00	0.55 ± 1.10
Liver	2.90 ± 0.14	23.54 ± 3.96	49.55 ± 2.74
Kidney	0.83 ± 0.18	6.83 ± 1.73	12.13 ± 1.19
Heart	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Lung	0.00 ± 0.00	0.59 ± 0.70	2.08 ± 0.55
Brain	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Adipose tissue	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Skeletal muscle	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Spleen	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Thymus	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Forestomach	0.13 ± 0.16	0.99 ± 1.97	2.33 ± 1.65
Glandular stomach	0.12 ± 0.20	2.76 ± 5.53	3.84 ± 1.42
Testes	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Preputial gland	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Seminal vesicle	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Skin (ear)	0.34 ± 0.30	0.00 ± 0.00	3.00 ± 0.89

^aData from three mice.

^bData from four mice.

Table 10: Concentration of [¹⁴C]NA equivalents in tissues of female mice at 72 hr after oral administration of [¹⁴C]NA

Tissue	Mean ± SD concentration (nmol/g)		
	20 mg/kg ^a	200 mg/kg ^b	500 mg/kg ^b
Plasma	0.07 ± 0.04	1.40 ± 0.67	1.99 ± 1.29
Blood cells	0.04 ± 0.08	0.00 ± 0.00	0.00 ± 0.00
Liver	3.67 ± 0.25	29.00 ± 2.74	67.49 ± 14.98
Kidney	0.56 ± 0.06	4.52 ± 0.98	7.91 ± 0.77
Heart	0.00 ± 0.00	0.00 ± 0.00	0.80 ± 1.11
Lung	0.00 ± 0.00	0.21 ± 0.42	2.14 ± 0.65
Brain	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Adipose tissue	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Skeletal muscle	0.00 ± 0.00	0.00 ± 0.00	0.83 ± 0.82
Spleen	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Thymus	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Forestomach	0.07 ± 0.10	0.69 ± 1.39	3.40 ± 2.16
Glandular stomach	0.11 ± 0.15	2.58 ± 3.26	4.63 ± 4.59
Ovary	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Clitoral gland	0.00 ± 0.00	0.00 ± 0.00	5.36 ± 6.30
Skin (ear)	0.00 ± 0.00	0.00 ± 0.00	4.73 ± 3.55

^aData from five mice.

^bData from four mice.

Table 11: Concentration of [¹⁴C]NA equivalents in tissues of male rats at 72 hr after oral administration of [¹⁴C]NA

Tissue	Mean ± SD concentration (nmol/g)		
	20 mg/kg ^a	200 mg/kg ^b	500 mg/kg ^b
Plasma	0.04 ± 0.05	0.20 ± 0.35	2.38 ± 1.52
Blood cells	0.03 ± 0.03	0.16 ± 0.28	0.85 ± 0.52
Liver	1.91 ± 0.19	19.89 ± 0.66	60.89 ± 3.80
Kidney	0.18 ± 0.02	1.77 ± 0.13	9.64 ± 8.83
Heart	0.00 ± 0.00	0.00 ± 0.00	1.10 ± 0.82
Lung	0.27 ± 0.05	1.38 ± 0.27	2.99 ± 0.67
Brain	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Adipose tissue	0.00 ± 0.00	0.00 ± 0.00	0.14 ± 0.25
Skeletal muscle	0.04 ± 0.06	0.00 ± 0.00	0.36 ± 0.37
Spleen	0.00 ± 0.00	0.14 ± 0.24	1.40 ± 1.34
Thymus	0.00 ± 0.00	0.00 ± 0.00	0.73 ± 0.80
Forestomach	0.01 ± 0.03	0.91 ± 0.68	1.57 ± 0.39
Glandular stomach	0.04 ± 0.03	0.99 ± 0.22	1.69 ± 0.53
Testes	0.00 ± 0.00	0.00 ± 0.00	0.67 ± 0.44
Preputial gland	0.93 ± 0.08	13.33 ± 2.13	43.55 ± 6.35
Seminal vesicle	0.00 ± 0.00	0.16 ± 0.27	0.76 ± 0.31
Skin (ear)	0.24 ± 0.06	1.45 ± 0.72	6.68 ± 4.34

^aData from four rats.

^bData from three rats.

Table 12: Concentration of [¹⁴C]NA equivalents in tissues of female rats at 72 hr after oral administration of [¹⁴C]NA

Tissue	Mean ± SD concentration (nmol/g) ^a		
	20 mg/kg	200 mg/kg	500 mg/kg
Plasma	0.00 ± 0.00	0.49 ± 0.33	5.19 ± 1.38
Blood cells	0.07 ± 0.11	0.13 ± 0.27	1.92 ± 0.72
Liver	2.00 ± 0.28	21.10 ± 2.61	86.65 ± 9.97
Kidney	0.20 ± 0.02	2.00 ± 0.31	20.54 ± 3.45
Heart	0.00 ± 0.00	0.00 ± 0.00	1.78 ± 0.58
Lung	0.21 ± 0.08	1.43 ± 0.17	5.07 ± 0.77
Brain	0.00 ± 0.00	0.00 ± 0.00	0.53 ± 0.16
Adipose tissue	0.00 ± 0.00	0.00 ± 0.00	0.41 ± 0.10
Skeletal muscle	0.00 ± 0.00	0.00 ± 0.00	0.91 ± 0.18
Spleen	0.00 ± 0.00	0.22 ± 0.26	3.19 ± 0.72
Thymus	0.00 ± 0.00	0.00 ± 0.00	1.62 ± 0.54
Forestomach	0.05 ± 0.04	0.31 ± 0.21	3.68 ± 0.74
Glandular stomach	0.03 ± 0.06	0.25 ± 0.29	3.63 ± 0.97
Ovary	0.00 ± 0.00	0.00 ± 0.00	2.43 ± 1.19
Clitoral gland	0.60 ± 0.71	7.52 ± 2.05	23.26 ± 8.77
Skin (ear)	0.22 ± 0.19	1.26 ± 0.69	10.99 ± 5.77

^aData from four rats.

Table 13: Percentage of the dose of ^{14}C radioactivity in tissues of male mice at 72 hr after oral administration of [^{14}C]NA^a

Tissue	Mean \pm SD fraction of dose (%)		
	20 mg/kg ^b	200 mg/kg ^c	500 mg/kg ^c
Plasma	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.01
Blood cells	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Liver	0.15 \pm 0.02	0.11 \pm 0.02	0.11 \pm 0.01
Kidney	0.02 \pm 0.01	0.01 \pm 0.00	0.01 \pm 0.00
Heart	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Lung	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Brain	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Adipose tissue	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Skeletal muscle	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Spleen	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Thymus	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Forestomach	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Glandular stomach	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Testes	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Preputial gland	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Seminal vesicle	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Skin (ear)	0.06 \pm 0.05	0.00 \pm 0.00	0.02 \pm 0.01
Total	0.22 \pm 0.06	0.12 \pm 0.02	0.15 \pm 0.01

^aPercentages were calculated from the organ weights and by assuming that plasma = 4%, blood cells = 4%, fat = 11%, skeletal muscle = 50%, and skin = 16% of body weight.

^bData from three mice.

^cData from four mice.

Table 14: Percentage of the dose of ^{14}C radioactivity in tissues of female mice at 72 hr after oral administration of $[^{14}\text{C}]\text{NA}^a$

Tissue	Mean \pm SD fraction of dose (%)		
	20 mg/kg ^b	200 mg/kg ^c	500 mg/kg ^c
Plasma	0.00 \pm 0.01	0.01 \pm 0.01	0.00 \pm 0.01
Blood cells	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Liver	0.20 \pm 0.03	0.15 \pm 0.02	0.16 \pm 0.02
Kidney	0.01 \pm 0.00	0.01 \pm 0.00	0.01 \pm 0.01
Heart	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Lung	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Brain	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Adipose tissue	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Skeletal muscle	0.00 \pm 0.00	0.00 \pm 0.00	0.02 \pm 0.02
Spleen	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Thymus	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Forestomach	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Glandular stomach	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Ovary	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Clitoral gland	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Skin (ear)	0.00 \pm 0.00	0.00 \pm 0.00	0.03 \pm 0.02
Total	0.22 \pm 0.02	0.16 \pm 0.02	0.22 \pm 0.06

^aPercentages were calculated from the organ weights and by assuming that plasma = 4%, blood cells = 4%, fat = 11%, skeletal muscle = 50%, and skin = 16% of body weight.

^bData from five mice.

^cData from four mice.

Table 15: Percentage of the dose of ^{14}C radioactivity in tissues of male rats at 72 hr after oral administration of [^{14}C]NA^a

Tissue	Mean \pm SD fraction of dose (%)		
	20 mg/kg ^b	200 mg/kg ^c	500 mg/kg ^c
Plasma	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.01
Blood cells	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Liver	0.08 \pm 0.01	0.10 \pm 0.01	0.12 \pm 0.01
Kidney	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.01
Heart	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Lung	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Brain	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Adipose tissue	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Skeletal muscle	0.02 \pm 0.03	0.00 \pm 0.00	0.01 \pm 0.01
Spleen	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Thymus	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Forestomach	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Glandular stomach	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Testes	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Preputial gland	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Seminal vesicle	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Skin (ear)	0.04 \pm 0.01	0.03 \pm 0.01	0.05 \pm 0.03
Total	0.14 \pm 0.03	0.13 \pm 0.01	0.19 \pm 0.06

^aPercentages were calculated from the organ weights and by assuming that plasma = 4%, blood cells = 4%, fat = 11%, skeletal muscle = 50%, and skin = 16% of body weight.

^bData from four rats.

^cData from three rats.

Table 16: Percentage of the dose of ^{14}C radioactivity in tissues of female rats at 72 hr after oral administration of [^{14}C]NA^a

Tissue	Mean \pm SD fraction of dose (%) ^b		
	20 mg/kg	200 mg/kg	500 mg/kg
Plasma	0.00 \pm 0.00	0.00 \pm 0.00	0.01 \pm 0.00
Blood cells	0.00 \pm 0.01	0.00 \pm 0.00	0.00 \pm 0.00
Liver	0.07 \pm 0.01	0.09 \pm 0.01	0.13 \pm 0.01
Kidney	0.00 \pm 0.00	0.00 \pm 0.00	0.01 \pm 0.00
Heart	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Lung	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Brain	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Adipose tissue	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Skeletal muscle	0.00 \pm 0.00	0.00 \pm 0.00	0.02 \pm 0.00
Spleen	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Thymus	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Forestomach	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Glandular stomach	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Ovary	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Clitoral gland	0.00 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00
Skin (ear)	0.04 \pm 0.03	0.02 \pm 0.02	0.08 \pm 0.05
Total	0.11 \pm 0.04	0.11 \pm 0.02	0.25 \pm 0.04

^aPercentages were calculated from the organ weights and by assuming that plasma = 4%, blood cells = 4%, fat = 11%, skeletal muscle = 50%, and skin = 16% of body weight.

^bData from four rats.

Table 17: Recovery of ¹⁴C radioactivity from male mice at 72 hr after oral administration of [¹⁴C]NA

Sample ^a	Mean ± SD dose recovered (%)		
	20 mg/kg	200 mg/kg	500 mg/kg
Urine	35.4 ± 2.9	45.7 ± 7.2	40.1 ± 6.4
Feces	36.7 ± 6.2	29.9 ± 5.7	33.6 ± 3.6
Cage rinse	13.3 ± 11.7	1.6 ± 0.1	3.2 ± 2.1
Tissues	0.3 ± 0.1	0.1 ± 0.0	0.2 ± 0.1
Total	85.7 ± 4.2	77.3 ± 8.6	76.9 ± 5.1

^aUrine and feces are expressed as the total cumulative % dose collected until the time of sacrifice at 72 hr. At sacrifice, tissues and cage rinse were collected.

Table 18: Recovery of ¹⁴C radioactivity from female mice at 72 hr after oral administration of [¹⁴C]NA

Sample ^a	Mean ± SD dose recovered (%)		
	20 mg/kg	200 mg/kg	500 mg/kg
Urine	46.3 ± 3.5	40.6 ± 0.7	35.9 ± 4.0
Feces	30.8 ± 4.5	34.5 ± 5.7	33.4 ± 3.6
Cage rinse	11.0 ± 4.9	3.4 ± 2.1	2.7 ± 0.9
Tissues	0.2 ± 0.0	0.2 ± 0.1	0.3 ± 0.1
Total	88.3 ± 1.7	78.7 ± 5.6	72.2 ± 1.2

^aUrine and feces are expressed as the total cumulative % dose collected until the time of sacrifice at 72 hr. At sacrifice, tissues and cage rinse were collected.

Table 19: Recovery of ¹⁴C radioactivity from male rats at 72 hr after oral administration of [¹⁴C]NA

Sample^a	Mean ± SD dose recovered (%)		
	20 mg/kg	200 mg/kg	500 mg/kg
Urine	79.1 ± 7.8	74.4 ± 4.6	61.2 ± 5.1
Feces	13.4 ± 2.3	18.8 ± 4.4	20.8 ± 4.5
Cage rinse	1.8 ± 1.8	1.0 ± 0.4	1.3 ± 0.4
Tissues	0.1 ± 0.1	0.1 ± 0.0	0.2 ± 0.1
Total	94.3 ± 8.4	94.3 ± 3.4	83.5 ± 1.7

^aUrine and feces are expressed as the total cumulative % dose collected until the time of sacrifice at 72 hr. At sacrifice, tissues and cage rinse were collected.

Table 20: Recovery of ¹⁴C radioactivity from female rats at 72 hr after oral administration of [¹⁴C]NA

Sample ^a	Mean ± SD dose recovered (%)		
	20 mg/kg	200 mg/kg	500 mg/kg
Urine	73.8 ± 4.7	72.1 ± 8.4	57.2 ± 7.6
Feces	11.8 ± 1.5	19.1 ± 3.7	31.4 ± 7.4
Cage rinse	1.6 ± 0.8	0.9 ± 0.7	2.3 ± 0.4
Tissues	0.1 ± 0.1	0.1 ± 0.0	0.3 ± 0.1
Total	87.3 ± 4.8	92.2 ± 5.3	91.1 ± 0.4

^aUrine and feces are expressed as the total cumulative % dose collected until the time of sacrifice at 72 hr. At sacrifice, tissues and cage rinse were collected.

Table 21: Effect of dose on the disposition and metabolism of [¹⁴C]NA in male and female mice

Parameter	20 mg/kg		200 mg/kg		500 mg/kg	
	males	females	males	females	males	females
	<i>Mean ± SD fraction of dose (%)</i>					
Minimum extent absorption	35.62	46.52	45.82	40.76	40.25	36.12
Excreted in urine						
0-24 hr	23.9 ± 10.1	35.7 ± 10.4	38.6 ± 10.6	30.5 ± 4.0	36.2 ± 6.6	25.4 ± 12.9
0-72 hr	35.4 ± 2.9	46.3 ± 3.5	45.7 ± 7.2	40.6 ± 0.7	40.1 ± 6.2	35.9 ± 4.0
Excreted in feces						
0-24 hr	23.3 ± 8.0	22.7 ± 6.0	21.2 ± 2.9	27.2 ± 7.4	29.1 ± 5.1	20.4 ± 12.9
0-72 hr	36.7 ± 6.2	30.8 ± 4.5	29.9 ± 5.7	34.5 ± 5.7	33.6 ± 3.6	33.4 ± 3.6
Tissues at 72 hr	0.22 ± 0.06	0.22 ± 0.02	0.12 ± 0.02	0.16 ± 0.02	0.15 ± 0.01	0.22 ± 0.06
Total recovery	85.7 ± 4.2	88.3 ± 1.7	77.3 ± 8.6	78.7 ± 5.6	76.9 ± 5.1	72.2 ± 1.2
Radioactivity excreted in urine as						
B (carboxynalidixic acid)	17.86	25.68	24.13	21.70	18.51	16.29
H	0.25	0.35	0.20	0.04	—	0.52
K (parent compound)	1.59	2.07	3.22	2.81	2.84	1.85
M	6.43	8.07	11.77	8.78	10.54	9.79

Table 22: Effect of dose on the disposition and metabolism of [¹⁴C]NA in male and female rats

Parameter	20 mg/kg		200 mg/kg		500 mg/kg	
	males	females	males	females	males	females
	<i>Mean ± SD fraction of dose (%)</i>					
Minimum extent absorption	79.24	73.91	74.53	72.21	61.39	57.45
Excreted in urine						
0-24 hr	74.1 ± 9.7	71.2 ± 4.8	60.4 ± 6.9	58.4 ± 14.7	26.3 ± 2.6	16.4 ± 5.8
0-72 hr	79.1 ± 7.8	73.8 ± 4.7	74.4 ± 4.6	72.1 ± 8.4	61.2 ± 5.1	57.2 ± 7.6
Excreted in feces						
0-24 hr	8.0 ± 2.0	7.7 ± 2.4	4.1 ± 2.1	2.3 ± 0.5	2.0 ± 1.4	2.6 ± 1.8
0-72 hr	13.4 ± 2.3	11.8 ± 1.5	18.8 ± 4.4	19.1 ± 3.7	20.8 ± 4.5	31.4 ± 7.4
Tissues at 72 hr	0.14 ± 0.03	0.11 ± 0.04	0.13 ± 0.01	0.11 ± 0.02	0.19 ± 0.06	0.25 ± 0.04
Total recovery	94.3 ± 8.4	87.3 ± 4.8	94.3 ± 3.4	92.2 ± 5.3	83.5 ± 1.7	91.1 ± 0.4
Radioactivity excreted in urine as						
B (carboxynalidixic acid)	58.61	52.06	41.26	44.07	26.77	23.33
H	10.07	9.44	16.26	8.97	20.27	10.05
K (parent compound)	5.24	8.68	10.33	10.56	5.41	5.13
M	0.99	0.52	0.18	1.78	0.49	0.43