ジフェニルアミンのラットを用いた
経口投与による2週間毒性試験（混餌試験）報告書

試験番号：0651

# TABLES

# TABLES

# TABLES (CONTINUED)

TABLE 1 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE RATS IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE

| Week-Day on Study | Control Av.Wt. | Control No.of Surviv. | 1600 ppm Av.Wt. | 1600 ppm % of cont. | 1600 ppm No.of Surviv. | 4000 ppm Av.Wt. | 4000 ppm % of cont. | 4000 ppm No.of Surviv. | 7000 ppm Av.Wt. | 7000 ppm % of cont. | 7000 ppm No.of Surviv. | 10000 ppm Av.Wt. | 10000 ppm % of cont. | 10000 ppm No.of Surviv. | 25000 ppm Av.Wt. | 25000 ppm % of cont. | 25000 ppm No.of Surviv. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | < 5> | | < 5> | | | < 5> | | | < 5> | | | < 5> | | | < 5> | | |
| 0-0 | 127 ( 5) | 5/ 5 | 127 ( 5) | 100 | 5/ 5 | 127 ( 5) | 100 | 5/ 5 | 127 ( 5) | 100 | 5/ 5 | 127 ( 5) | 100 | 5/ 5 | 127 ( 5) | 100 | 5/ 5 |
| 1-4 | 143 ( 5) | 5/ 5 | 144 ( 5) | 101 | 5/ 5 | 140 ( 5) | 98 | 5/ 5 | 134 ( 5) | 94 | 5/ 5 | 123 ( 5) | 86 | 5/ 5 | 92 ( 5) | 64 | 5/ 5 |
| 1-7 | 157 ( 5) | 5/ 5 | 155 ( 5) | 99 | 5/ 5 | 153 ( 5) | 97 | 5/ 5 | 143 ( 5) | 91 | 5/ 5 | 137 ( 5) | 87 | 5/ 5 | 103 ( 4) | 66 | 4/ 5 |
| 2-4 | 176 ( 5) | 5/ 5 | 175 ( 5) | 99 | 5/ 5 | 167 ( 5) | 95 | 5/ 5 | 160 ( 5) | 91 | 5/ 5 | 154 ( 5) | 88 | 5/ 5 | 108 ( 4) | 61 | 4/ 5 |
| 2-7 | 186 ( 5) | 5/ 5 | 185 ( 5) | 99 | 5/ 5 | 177 ( 5) | 95 | 5/ 5 | 173 ( 5) | 93 | 5/ 5 | 164 ( 5) | 88 | 5/ 5 | 113 ( 4) | 61 | 4/ 5 |

< > : No. of effective animals, ( ) : No. of measured animals Av.Wt. : Averaged body weight (Unit : g).

TABLE 2 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE RATS IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE

| Week-Day on Study | Control Av.Wt. | Control No.of Surviv. | 1600 ppm Av.Wt. | 1600 ppm % of cont. | 1600 ppm No.of Surviv. | 4000 ppm Av.Wt. | 4000 ppm % of cont. | 4000 ppm No.of Surviv. | 7000 ppm Av.Wt. | 7000 ppm % of cont. | 7000 ppm No.of Surviv. | 10000 ppm Av.Wt. | 10000 ppm % of cont. | 10000 ppm No.of Surviv. | 25000 ppm Av.Wt. | 25000 ppm % of cont. | 25000 ppm No.of Surviv. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | < 5> | | < 5> | | | < 5> | | | < 5> | | | < 5> | | | < 5> | | |
| 0-0 | 100 ( 5) | 5/ 5 | 100 ( 5) | 100 | 5/ 5 | 100 ( 5) | 100 | 5/ 5 | 99 ( 5) | 99 | 5/ 5 | 100 ( 5) | 100 | 5/ 5 | 100 ( 5) | 100 | 5/ 5 |
| 1-4 | 108 ( 5) | 5/ 5 | 109 ( 5) | 101 | 5/ 5 | 105 ( 5) | 97 | 5/ 5 | 102 ( 5) | 94 | 5/ 5 | 99 ( 5) | 92 | 5/ 5 | 74 ( 5) | 69 | 5/ 5 |
| 1-7 | 115 ( 5) | 5/ 5 | 114 ( 5) | 99 | 5/ 5 | 109 ( 5) | 95 | 5/ 5 | 107 ( 5) | 93 | 5/ 5 | 104 ( 5) | 90 | 5/ 5 | 80 ( 3) | 70 | 3/ 5 |
| 2-4 | 124 ( 5) | 5/ 5 | 122 ( 5) | 98 | 5/ 5 | 117 ( 5) | 94 | 5/ 5 | 114 ( 5) | 92 | 5/ 5 | 113 ( 5) | 91 | 5/ 5 | 85 ( 3) | 69 | 3/ 5 |
| 2-7 | 126 ( 5) | 5/ 5 | 124 ( 5) | 98 | 5/ 5 | 120 ( 5) | 95 | 5/ 5 | 118 ( 5) | 94 | 5/ 5 | 118 ( 5) | 94 | 5/ 5 | 87 ( 3) | 69 | 3/ 5 |

< > : No. of effective animals, ( ) : No. of measured animals Av.Wt. : Averaged body weight (Unit : g).

TABLE 3 FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE

| Week-Day on Study | Control | | 1600 ppm | | | 4000 ppm | | | 7000 ppm | | | 10000 ppm | | | 25000 ppm | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Av.Fc. | No.of Surviv. | Av.Fc. | % of cont. | No.of Surviv. | Av.Fc. | % of cont. | No.of Surviv. | Av.Fc. | % of cont. | No.of Surviv. | Av.Fc. | % of cont. | No.of Surviv. | Av.Fc. | % of cont. | No.of Surviv. |
| | < 5> | | < 5> | | | < 5> | | | < 5> | | | < 5> | | | < 5> | | |
| 1-4 | 13.0 ( 5) | 5/ 5 | 12.6 ( 5) | 97 | 5/ 5 | 11.5 ( 5) | 88 | 5/ 5 | 9.7 ( 5) | 75 | 5/ 5 | 8.0 ( 5) | 62 | 5/ 5 | 4.4 ( 5) | 34 | 5/ 5 |
| 1-7 | 13.7 ( 5) | 5/ 5 | 13.3 ( 5) | 97 | 5/ 5 | 13.3 ( 5) | 97 | 5/ 5 | 12.6 ( 5) | 92 | 5/ 5 | 12.8 ( 5) | 93 | 5/ 5 | 8.8 ( 4) | 64 | 4/ 5 |
| 2-4 | 14.0 ( 5) | 5/ 5 | 13.8 ( 5) | 99 | 5/ 5 | 13.3 ( 5) | 95 | 5/ 5 | 13.4 ( 5) | 96 | 5/ 5 | 13.0 ( 5) | 93 | 5/ 5 | 8.4 ( 4) | 60 | 4/ 5 |
| 2-7 | 14.2 ( 5) | 5/ 5 | 14.1 ( 5) | 99 | 5/ 5 | 13.9 ( 5) | 98 | 5/ 5 | 13.5 ( 5) | 95 | 5/ 5 | 13.2 ( 5) | 93 | 5/ 5 | 10.2 ( 4) | 72 | 4/ 5 |

< > : No. of effective animals, ( ) : No. of measured animals Av.Fc. : Averaged food consumption (Unit : g).

TABLE 4 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE

| Week-Day on Study | Control | | 1600 ppm | | | 4000 ppm | | | 7000 ppm | | | 10000 ppm | | | 25000 ppm | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Av.Fc. | No.of Surviv. | Av.Fc. | % of cont. | No.of Surviv. | Av.Fc. | % of cont. | No.of Surviv. | Av.Fc. | % of cont. | No.of Surviv. | Av.Fc. | % of cont. | No.of Surviv. | Av.Fc. | % of cont. | No.of Surviv. |
| | < 5> | | < 5> | | | < 5> | | | < 5> | | | < 5> | | | < 5> | | |
| 1-4 | 9.9 ( 5) | 5/ 5 | 9.7 ( 5) | 98 | 5/ 5 | 8.3 ( 5) | 84 | 5/ 5 | 7.6 ( 5) | 77 | 5/ 5 | 6.5 ( 5) | 66 | 5/ 5 | 3.0 ( 4) | 30 | 5/ 5 |
| 1-7 | 10.2 ( 5) | 5/ 5 | 10.0 ( 5) | 98 | 5/ 5 | 9.6 ( 5) | 94 | 5/ 5 | 9.4 ( 5) | 92 | 5/ 5 | 9.6 ( 5) | 94 | 5/ 5 | 8.6 ( 3) | 84 | 3/ 5 |
| 2-4 | 10.4 ( 5) | 5/ 5 | 10.0 ( 5) | 96 | 5/ 5 | 9.7 ( 5) | 93 | 5/ 5 | 9.3 ( 5) | 89 | 5/ 5 | 8.9 ( 5) | 86 | 5/ 5 | 9.2 ( 3) | 88 | 3/ 5 |
| 2-7 | 10.2 ( 5) | 5/ 5 | 9.8 ( 5) | 96 | 5/ 5 | 9.5 ( 5) | 93 | 5/ 5 | 9.1 ( 5) | 89 | 5/ 5 | 9.2 ( 5) | 90 | 5/ 5 | 9.8 ( 3) | 96 | 3/ 5 |

< > : No. of effective animals, ( ) : No. of measured animals Av.Fc. : Averaged food consumption (Unit : g).

TABLE 5 HEMATOLOGY OF MALE RATS IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE

| Group Name | Control | 1600 ppm | 4000 ppm | 7000 ppm | 10000 ppm | 25000 ppm |
|---|---|---|---|---|---|---|
| No. of examined animals | 5 | 5 | 5 | 5 | 5 | 4 |
| RED BLOOD CELL ($10^6/\mu$ L) | 7.90 ± 0.13 | 7.61 ± 0.09 ** | 6.47 ± 0.13 ** | 5.92 ± 0.09 ** | 5.86 ± 0.13 ** | 5.06 ± 0.13 ** |
| HEMOGLOBIN (g/dL) | 15.4 ± 0.2 | 14.8 ± 0.1 ** | 13.8 ± 0.1 ** | 14.0 ± 0.3 ** | 14.3 ± 0.1 ** | 12.9 ± 0.2 ** |
| HEMATOCRIT (%) | 41.0 ± 0.7 | 39.5 ± 0.4 ** | 38.1 ± 0.3 ** | 40.0 ± 0.9 * | 41.4 ± 0.3 | 38.1 ± 0.4 ** |
| MCV (fL) | 51.8 ± 0.2 | 51.9 ± 0.6 | 58.9 ± 1.3 ** | 67.6 ± 1.5 ** | 70.8 ± 1.4 ** | 75.4 ± 1.3 ** |
| MCH (pg) | 19.5 ± 0.2 | 19.4 ± 0.1 | 21.3 ± 0.3 ** | 23.6 ± 0.4 ** | 24.4 ± 0.4 ** | 25.5 ± 0.5 ** |
| MCHC (g/dL) | 37.5 ± 0.4 | 37.4 ± 0.3 | 36.2 ± 0.3 ** | 35.0 ± 0.7 ** | 34.6 ± 0.4 ** | 33.8 ± 0.5 ** |
| PLATELET ($10^3/\mu$ L) | 858 ± 56 | 943 ± 44 ** | 944 ± 14 ** | 890 ± 17 | 875 ± 43 | 874 ± 19 |
| RETICULOCYTE (%) | 3.9 ± 0.3 | 5.3 ± 0.6 ** | 12.6 ± 1.1 ** | 16.1 ± 0.8 ** | 17.2 ± 1.4 ** | 28.2 ± 3.6 ** |
| METHEMOGLOBIN (%) | 0.5 ± 0.1 | 1.2 ± 0.6 | 3.3 ± 0.8 ** | 2.2 ± 0.4 ** | 2.8 ± 0.9 ** | 7.2 ± 3.7 ** |
| WBC ($10^3/\mu$ L) | 5.48 ± 0.44 | 7.03 ± 0.78 | 7.56 ± 0.57 * | 7.47 ± 0.89 * | 7.39 ± 1.65 * | 7.24 ± 1.08 |

Mean ± S.D.

Significant difference: * : $p \leqq 0.05$ ** : $p \leqq 0.01$ Test of Dunnett

TABLE 6 HEMATOLOGY OF FEMALE RATS IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE

| Group Name | Control | 1600 ppm | 4000 ppm | 7000 ppm | 10000 ppm | 25000 ppm |
|---|---|---|---|---|---|---|
| No. of examined animals | 5 | 5 | 5 | 5 | 5 | 3 |
| RED BLOOD CELL ($10^6/\mu$ L) | 8.33 ± 0.24 | 7.44 ± 0.19 ** | 6.37 ± 0.10 ** | 6.03 ± 0.27 ** | 5.76 ± 0.23 ** | 4.79 ± 0.36 ** |
| HEMOGLOBIN (g/dL) | 16.2 ± 0.5 | 14.5 ± 0.3 ** | 13.7 ± 0.2 ** | 13.8 ± 0.5 ** | 13.7 ± 0.4 ** | 12.5 ± 0.7 ** |
| HEMATOCRIT (%) | 42.0 ± 1.1 | 38.1 ± 0.9 ** | 37.0 ± 0.9 ** | 38.9 ± 1.3 ** | 39.2 ± 1.1 ** | 37.1 ± 1.5 ** |
| MCV (fL) | 50.4 ± 0.3 | 51.3 ± 0.3 ** | 58.1 ± 1.5 ** | 64.6 ± 1.3 ** | 68.1 ± 0.9 ** | 77.6 ± 2.8 ** |
| MCH (pg) | 19.4 ± 0.1 | 19.6 ± 0.1 * | 21.4 ± 0.3 ** | 22.9 ± 0.5 ** | 23.9 ± 0.4 ** | 26.1 ± 0.7 ** |
| MCHC (g/dL) | 38.6 ± 0.3 | 38.2 ± 0.2 | 36.9 ± 0.4 ** | 35.5 ± 0.1 ** | 35.1 ± 0.2 ** | 33.6 ± 0.6 ** |
| RETICULOCYTE (%) | 2.0 ± 0.2 | 5.0 ± 0.3 ** | 12.8 ± 0.9 ** | 16.3 ± 1.1 ** | 16.3 ± 1.5 ** | 23.7 ± 4.8 ** |
| METHEMOGLOBIN (%) | 0.4 ± 0.2 | 1.4 ± 0.4 | 2.4 ± 0.3 ** | 2.0 ± 0.5 ** | 2.5 ± 1.1 ** | 6.4 ± 1.0 ** |
| WBC ($10^3/\mu$ L) | 5.62 ± 1.68 | 6.63 ± 0.54 | 8.11 ± 1.42 * | 7.49 ± 1.72 | 8.27 ± 1.26 * | 8.08 ± 0.86 |

Mean ± S.D.

Significant difference: * : $p \leqq 0.05$ ** : $p \leqq 0.01$ Test of Dunnett

TABLE 7 BIOCHEMISTRY OF MALE RATS IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE

| Group Name | Control | 1600 ppm | | 4000 ppm | | 7000 ppm | | 10000 ppm | | 25000 ppm | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| No. of examined animals | 5 | 5 | | 5 | | 5 | | 5 | | 4 | |
| TOTAL PROTEIN (g/dL) | 5.7 ± 0.1 | 6.0 ± 0.1 | * | 6.3 ± 0.1 | ** | 6.3 ± 0.1 | ** | 6.3 ± 0.2 | ** | 7.0 ± 0.2 | ** |
| ALBUMIN (g/dL) | 3.3 ± 0.1 | 3.6 ± 0.2 | ** | 4.0 ± 0.1 | ** | 4.0 ± 0.1 | ** | 4.1 ± 0.2 | ** | 4.7 ± 0.1 | ** |
| A/G RATIO | 1.4 ± 0.0 | 1.6 ± 0.2 | | 1.8 ± 0.2 | ** | 1.8 ± 0.1 | ** | 1.8 ± 0.1 | ** | 2.0 ± 0.1 | ** |
| T-BILIRUBIN (mg/dL) | 0.10 ± 0.01 | 0.13 ± 0.01 | | 0.20 ± 0.02 | ** | 0.22 ± 0.02 | ** | 0.26 ± 0.03 | ** | 0.38 ± 0.02 | ** |
| GLUCOSE (mg/dL) | 193 ± 4 | 195 ± 10 | | 190 ± 5 | | 175 ± 13 | ** | 166 ± 5 | ** | 129 ± 4 | ** |
| T-CHOLESTEROL (mg/dL) | 66 ± 2 | 61 ± 5 | | 71 ± 5 | | 84 ± 3 | ** | 92 ± 6 | ** | 106 ± 9 | ** |
| PHOSPHOLIPID (mg/dL) | 136 ± 8 | 130 ± 5 | | 145 ± 8 | | 159 ± 5 | ** | 170 ± 9 | ** | 196 ± 18 | ** |
| ALT (IU/L) | 35 ± 9 | 33 ± 4 | | 37 ± 9 | | 33 ± 3 | | 35 ± 3 | | 73 ± 9 | ** |
| LDH (IU/L) | 203 ± 6 | 212 ± 12 | | 251 ± 64 | | 225 ± 28 | | 262 ± 33 | * | 373 ± 67 | ** |
| UREA NITOROGEN (mg/dL) | 16.0 ± 1.2 | 18.4 ± 2.7 | | 19.1 ± 2.0 | * | 19.1 ± 1.1 | * | 19.2 ± 0.7 | ** | 23.9 ± 3.6 | ** |
| POTASSIUM (mEq/L) | 3.9 ± 0.3 | 3.6 ± 0.1 | | 3.6 ± 0.3 | | 3.7 ± 0.2 | | 3.9 ± 0.2 | | 4.8 ± 0.5 | ** |
| CALCIUM (mg/dL) | 11.0 ± 0.2 | 11.1 ± 0.1 | | 11.1 ± 0.2 | | 11.1 ± 0.1 | | 10.9 ± 0.3 | | 11.5 ± 0.1 | ** |

Mean ± S.D.

Significant difference: * : p≦0.05 ** : p≦0.01 Test of Dunnett

TABLE 8 BIOCHEMISTRY OF FEMALE RATS IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE

| Group Name | Control | 1600 ppm | | 4000 ppm | | 7000 ppm | | 10000 ppm | | 25000 ppm | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| No. of examined animals | 5 | 5 | | 5 | | 5 | | 5 | | 3 | |
| TOTAL PROTEIN (g/dL) | 5.6 ± 0.2 | 5.9 ± 0.1 | * | 6.1 ± 0.2 | ** | 6.2 ± 0.1 | ** | 6.2 ± 0.0 | ** | 6.8 ± 0.2 | ** |
| ALBUMIN (g/dL) | 3.4 ± 0.1 | 3.8 ± 0.1 | ** | 4.0 ± 0.1 | ** | 4.1 ± 0.1 | ** | 4.1 ± 0.0 | ** | 4.6 ± 0.1 | ** |
| A/G RATIO | 1.5 ± 0.1 | 1.8 ± 0.1 | ** | 1.8 ± 0.1 | ** | 1.9 ± 0.1 | ** | 2.0 ± 0.0 | ** | 2.1 ± 0.1 | ** |
| T-BILIRUBIN (mg/dL) | 0.10 ± 0.01 | 0.15 ± 0.01 | * | 0.18 ± 0.01 | ** | 0.20 ± 0.02 | ** | 0.23 ± 0.04 | ** | 0.48 ± 0.13 | ** |
| GLUCOSE (mg/dL) | 186 ± 11 | 179 ± 7 | | 173 ± 10 | | 165 ± 10 | | 165 ± 10 | | 117 ± 27 | ** |
| T-CHOLESTEROL (mg/dL) | 74 ± 5 | 64 ± 3 | * | 74 ± 5 | | 84 ± 6 | * | 95 ± 7 | ** | 106 ± 5 | ** |
| PHOSPHOLIPID (mg/dL) | 144 ± 6 | 124 ± 5 | ** | 140 ± 8 | | 154 ± 8 | | 175 ± 11 | ** | 207 ± 11 | ** |
| AST (IU/L) | 62 ± 3 | 66 ± 7 | | 66 ± 3 | | 63 ± 3 | | 63 ± 7 | | 107 ± 30 | |
| ALT (IU/L) | 28 ± 3 | 30 ± 5 | | 29 ± 3 | | 32 ± 4 | | 34 ± 7 | | 94 ± 35 | ** |
| LDH (IU/L) | 306 ± 32 | 308 ± 62 | | 352 ± 113 | | 345 ± 99 | | 307 ± 43 | | 544 ± 138 | ** |
| UREA NITOROGEN (mg/dL) | 17.7 ± 2.4 | 20.0 ± 2.1 | | 20.1 ± 2.2 | | 20.7 ± 1.2 | | 22.0 ± 2.7 | * | 27.5 ± 2.9 | ** |
| POTASSIUM (mEq/L) | 3.9 ± 0.2 | 3.6 ± 0.2 | | 3.7 ± 0.3 | | 3.8 ± 0.2 | | 3.8 ± 0.3 | | 4.6 ± 0.2 | ** |
| CALCIUM (mg/dL) | 10.7 ± 0.2 | 10.7 ± 0.2 | | 10.8 ± 0.2 | | 10.8 ± 0.1 | | 10.7 ± 0.1 | | 11.6 ± 0.3 | ** |

Mean ± S.D.

Significant difference: * : p≦0.05 ** : p≦0.01 Test of Dunnett

TABLE 9 URINALYSIS OF MALE RATS IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE

| Group Name | | Control | 1600 ppm | 4000 ppm | 7000 ppm | 10000 ppm | 25000 ppm |
|---|---|---|---|---|---|---|---|
| No. of examined animals | | 5 | 5 | 5 | 5 | 5 | 4 |
| | Grade | | | | | | |
| pH | 5.0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6.0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6.5 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 7.0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 7.5 | 0 | 0 | 0 | 0 | 1 | 2 |
| | 8.0 | 2 | 2 | 3 | 3 | 3 | 1 |
| | 8.5 | 3 | 3 | 2 | 2 | 1 | 0 |
| Protein | − | 0 | 0 | 0 | 0 | 0 | 1 |
| | ± | 0 | 0 | 0 | 1 | 2 | 2 |
| | + | 2 | 2 | 4 | 2 | 2 | 1 |
| | 2+ | 3 | 3 | 1 | 2 | 1 | 0 |
| | 3+ | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4+ | 0 | 0 | 0 | 0 | 0 | 0 |

TABLE 10 URINALYSIS OF FEMALE RATS IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE

| Group Name | | Control | 1600 ppm | 4000 ppm | 7000 ppm | 10000 ppm | 25000 ppm |
|---|---|---|---|---|---|---|---|
| No. of examined animals | | 5 | 5 | 5 | 5 | 5 | 3 |
| | Grade | | | | | | |
| pH | 5.0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6.0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6.5 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 7.0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 7.5 | 0 | 0 | 0 | 0 | 0 | 3 |
| | 8.0 | 3 | 2 | 1 | 4 | 4 | 0 |
| | 8.5 | 2 | 3 | 4 | 1 | 1 | 0 |

TABLE 11 ORGAN WEIGHTS OF MALE RATS IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE

| Group Name | Control | 1600 ppm | 4000 ppm | 7000 ppm | 10000 ppm | 25000 ppm |
|---|---|---|---|---|---|---|
| No. of examined animal | 5 | 5 | 5 | 5 | 5 | 4 |
| Body weight (g) | 186 ± 9 | 185 ± 7 | 177 ± 9 | 173 ± 6 * | 164 ± 5 ** | 113 ± 5 ** |
| Thymus (g) | 0.352 ± 0.021 | 0.365 ± 0.029 | 0.335 ± 0.012 | 0.335 ± 0.027 | 0.291 ± 0.007 ** | 0.123 ± 0.026 ** |
| Thymus (%) | 0.189 ± 0.014 | 0.197 ± 0.011 | 0.189 ± 0.006 | 0.194 ± 0.015 | 0.178 ± 0.008 | 0.108 ± 0.019 ** |
| Adrenals (g) | 0.034 ± 0.003 | 0.034 ± 0.003 | 0.033 ± 0.002 | 0.033 ± 0.003 | 0.032 ± 0.003 | 0.029 ± 0.003 |
| Adrenals (%) | 0.018 ± 0.001 | 0.019 ± 0.001 | 0.019 ± 0.001 | 0.019 ± 0.001 | 0.019 ± 0.002 | 0.026 ± 0.003 ** |
| Testes (g) | 2.380 ± 0.153 | 2.254 ± 0.053 | 2.289 ± 0.165 | 2.301 ± 0.089 | 2.219 ± 0.260 | 1.294 ± 0.375 ** |
| Testes (%) | 1.279 ± 0.043 | 1.220 ± 0.053 | 1.289 ± 0.035 | 1.330 ± 0.062 | 1.350 ± 0.124 | 1.141 ± 0.306 |
| Heart (g) | 0.661 ± 0.022 | 0.659 ± 0.039 | 0.654 ± 0.031 | 0.624 ± 0.016 | 0.612 ± 0.024 * | 0.451 ± 0.024 ** |
| Heart (%) | 0.356 ± 0.011 | 0.356 ± 0.011 | 0.369 ± 0.002 | 0.361 ± 0.012 | 0.373 ± 0.005 * | 0.400 ± 0.022 ** |
| Lungs (g) | 0.744 ± 0.030 | 0.744 ± 0.042 | 0.728 ± 0.035 | 0.716 ± 0.029 | 0.661 ± 0.032 ** | 0.535 ± 0.015 ** |
| Lungs (%) | 0.400 ± 0.012 | 0.402 ± 0.014 | 0.410 ± 0.011 | 0.414 ± 0.015 | 0.403 ± 0.009 | 0.475 ± 0.024 ** |
| Kidneys (g) | 1.392 ± 0.085 | 1.460 ± 0.046 | 1.482 ± 0.067 | 1.464 ± 0.060 | 1.437 ± 0.075 | 1.154 ± 0.020 ** |
| Kidneys (%) | 0.748 ± 0.025 | 0.789 ± 0.017 | 0.835 ± 0.027 ** | 0.846 ± 0.023 ** | 0.875 ± 0.022 ** | 1.025 ± 0.033 ** |
| Spleen (g) | 0.458 ± 0.024 | 0.531 ± 0.039 * | 0.844 ± 0.053 ** | 0.921 ± 0.064 ** | 0.837 ± 0.018 ** | 0.581 ± 0.037 ** |
| Spleen (%) | 0.246 ± 0.005 | 0.287 ± 0.017 ** | 0.476 ± 0.014 ** | 0.531 ± 0.018 ** | 0.511 ± 0.021 ** | 0.515 ± 0.019 ** |
| Liver (g) | 7.041 ± 0.594 | 8.572 ± 0.409 ** | 9.199 ± 0.695 ** | 9.216 ± 0.567 ** | 8.917 ± 0.537 ** | 7.040 ± 0.384 |
| Liver (%) | 3.781 ± 0.165 | 4.638 ± 0.260 ** | 5.180 ± 0.175 ** | 5.318 ± 0.153 ** | 5.434 ± 0.199 ** | 6.243 ± 0.122 ** |
| Brain (g) | 1.748 ± 0.034 | 1.756 ± 0.027 | 1.744 ± 0.035 | 1.724 ± 0.051 | 1.723 ± 0.018 | 1.630 ± 0.027 ** |
| Brain (%) | 0.942 ± 0.048 | 0.950 ± 0.021 | 0.984 ± 0.039 | 0.997 ± 0.042 | 1.051 ± 0.022 ** | 1.448 ± 0.083 ** |

Mean ± S.D.

Significant difference: * : $p \leqq 0.05$ ** : $p \leqq 0.01$ Test of Dunnett

TABLE 12 ORGAN WEIGHTS OF FEMALE RATS IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE

| Group Name | Control | 1600 ppm | 4000 ppm | 7000 ppm | 10000 ppm | 25000 ppm |
|---|---|---|---|---|---|---|
| No. of examined animal | 5 | 5 | 5 | 5 | 5 | 3 |
| Body weight (g) | 126 ± 6 | 124 ± 4 | 120 ± 4 | 118 ± 6 | 118 ± 7 | 87 ± 8 ** |
| Thymus (g) | 0.274 ± 0.018 | 0.280 ± 0.018 | 0.277 ± 0.013 | 0.260 ± 0.017 | 0.285 ± 0.015 | 0.092 ± 0.033 ** |
| Thymus (%) | 0.217 ± 0.017 | 0.225 ± 0.009 | 0.231 ± 0.008 | 0.221 ± 0.020 | 0.242 ± 0.006 ** | 0.104 ± 0.030 |
| Adrenals (g) | 0.042 ± 0.002 | 0.039 ± 0.002 | 0.037 ± 0.005 | 0.034 ± 0.001 ** | 0.031 ± 0.002 ** | 0.030 ± 0.003 ** |
| Adrenals (%) | 0.033 ± 0.001 | 0.032 ± 0.001 | 0.031 ± 0.005 | 0.029 ± 0.000 * | 0.026 ± 0.001 ** | 0.035 ± 0.006 |
| Ovaries (g) | 0.053 ± 0.005 | 0.048 ± 0.005 | 0.047 ± 0.006 | 0.042 ± 0.005 | 0.037 ± 0.011 ** | 0.022 ± 0.003 ** |
| Ovaries (%) | 0.042 ± 0.004 | 0.038 ± 0.004 | 0.039 ± 0.004 | 0.035 ± 0.005 | 0.031 ± 0.008 * | 0.026 ± 0.003 ** |
| Heart (g) | 0.475 ± 0.022 | 0.489 ± 0.025 | 0.480 ± 0.017 | 0.453 ± 0.042 | 0.449 ± 0.028 | 0.356 ± 0.039 ** |
| Heart (%) | 0.376 ± 0.019 | 0.393 ± 0.020 | 0.401 ± 0.016 | 0.384 ± 0.021 | 0.382 ± 0.021 | 0.410 ± 0.018 |
| Lungs (g) | 0.592 ± 0.028 | 0.585 ± 0.016 | 0.570 ± 0.027 | 0.551 ± 0.025 | 0.540 ± 0.030 * | 0.449 ± 0.017 ** |
| Lungs (%) | 0.469 ± 0.023 | 0.470 ± 0.010 | 0.476 ± 0.015 | 0.468 ± 0.023 | 0.458 ± 0.011 | 0.519 ± 0.028 ** |
| Kidneys (g) | 0.971 ± 0.043 | 0.997 ± 0.036 | 0.996 ± 0.063 | 1.017 ± 0.062 | 1.001 ± 0.056 | 0.871 ± 0.070 |
| Kidneys (%) | 0.768 ± 0.024 | 0.801 ± 0.027 | 0.832 ± 0.041 * | 0.864 ± 0.042 ** | 0.851 ± 0.024 ** | 1.006 ± 0.059 ** |
| Spleen (g) | 0.327 ± 0.020 | 0.421 ± 0.027 ** | 0.626 ± 0.028 ** | 0.652 ± 0.060 ** | 0.633 ± 0.040 ** | 0.469 ± 0.053 ** |
| Spleen (%) | 0.258 ± 0.013 | 0.338 ± 0.017 ** | 0.523 ± 0.013 ** | 0.553 ± 0.031 ** | 0.538 ± 0.022 ** | 0.540 ± 0.023 ** |
| Liver (g) | 4.483 ± 0.200 | 5.334 ± 0.177 ** | 5.583 ± 0.162 ** | 5.645 ± 0.432 ** | 5.890 ± 0.192 ** | 5.089 ± 0.228 * |
| Liver (%) | 3.549 ± 0.145 | 4.288 ± 0.132 ** | 4.662 ± 0.091 ** | 4.790 ± 0.237 ** | 5.008 ± 0.206 ** | 5.889 ± 0.311 ** |
| Brain (g) | 1.635 ± 0.019 | 1.627 ± 0.019 | 1.587 ± 0.043 | 1.595 ± 0.040 | 1.589 ± 0.033 | 1.530 ± 0.022 ** |
| Brain (%) | 1.295 ± 0.055 | 1.309 ± 0.032 | 1.325 ± 0.028 | 1.355 ± 0.032 | 1.351 ± 0.055 | 1.777 ± 0.189 ** |

Mean ± S.D.

Significant difference: * : $p \leqq 0.05$ ** : $p \leqq 0.01$ Test of Dunnett

TABLE 13 INCIDENCES OF SELECTED LESIONS OF MALE RATS IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE (DEAD AND MORIBUND ANIMALS)

| Group Name | Control | | | | 1600 ppm | | | | 4000 ppm | | | | 7000 ppm | | | | 10000 ppm | | | | 25000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Number of examined animals | 0 | | | | 0 | | | | 0 | | | | 0 | | | | 0 | | | | 1 | | | |
| Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| spleen | | | | | | | | | | | | | | | | | | | | | <1> | | | |
| atrophy | — | | | | — | | | | — | | | | — | | | | — | | | | 0 | 1 | 0 | 0 |
| engorgement of erythrocyte | — | | | | — | | | | — | | | | — | | | | — | | | | 1 | 0 | 0 | 0 |
| kidney | | | | | | | | | | | | | | | | | | | | | <1> | | | |
| tubular necrosis | — | | | | — | | | | — | | | | — | | | | — | | | | 0 | 1 | 0 | 0 |

Grade 1: Slight 2 : Moderate 3 : Marked 4 :Severe
< > : Number of animals examined at the site
— : All animals survived at the terminal necropsy

TABLE 14 INCIDENCES OF SELECTED LESIONS OF MALE RATS IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE (SACRIFICED ANIMALS)

| Group Name | Control | | | | 1600 ppm | | | | 4000 ppm | | | | 7000 ppm | | | | 10000 ppm | | | | 25000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Number of examined animals | 5 | | | | 5 | | | | 5 | | | | 5 | | | | 5 | | | | 4 | | | |
| Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| spleen | <5> | | | | <5> | | | | <5> | | | | <5> | | | | <5> | | | | <4> | | | |
| deposit of hemosiderin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 1 | 3 | 0 | 0 |
| extramedullary hematopoiesis | 0 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 4 | 0 | 0 |
| engorgement of erythrocyte | 0 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 4 | 0 | 0 |
| liver | <5> | | | | <5> | | | | <5> | | | | <5> | | | | <5> | | | | <4> | | | |
| necrosis:single cell | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| hepatocellular hypertrophy:central | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 4 | 0 | 0 |

Grade 1: Slight 2 : Moderate 3 : Marked 4 :Severe
< > : Number of animals examined at the site

TABLE 15 INCIDENCES OF SELECTED LESIONS OF FEMALE RATS IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE (DEAD AND MORIBUND ANIMALS)

| Group Name | Control | | | | 1600 ppm | | | | 4000 ppm | | | | 7000 ppm | | | | 10000 ppm | | | | 25000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Number of examined animals | 0 | | | | 0 | | | | 0 | | | | 0 | | | | 0 | | | | 2 | | | |
| Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| spleen | | | | | | | | | | | | | | | | | | | | | | <2> | | |
| atrophy | | | — | | | | — | | | | — | | | | — | | | | — | | 0 | 2 | 0 | 0 |
| liver | | | | | | | | | | | | | | | | | | | | | | <2> | | |
| necrosis:central | | | — | | | | — | | | | — | | | | — | | | | — | | 2 | 0 | 0 | 0 |
| kidney | | | | | | | | | | | | | | | | | | | | | | <2> | | |
| tubular necrosis | | | — | | | | — | | | | — | | | | — | | | | — | | 0 | 2 | 0 | 0 |

Grade 1: Slight 2 : Moderate 3 : Marked 4 :Severe
< > : Number of animals examined at the site
— : All animals survived at the terminal necropsy

TABLE 16 INCIDENCES OF SELECTED LESIONS OF FEMALE RATS IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE (SACRIFICED ANIMALS)

| Group Name | Control | | | | 1600 ppm | | | | 4000 ppm | | | | 7000 ppm | | | | 10000 ppm | | | | 25000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Number of examined animals | 5 | | | | 5 | | | | 5 | | | | 5 | | | | 5 | | | | 3 | | | |
| Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| spleen | <5> | | | | <5> | | | | <5> | | | | <5> | | | | <5> | | | | <3> | | | |
| deposit of hemosiderin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 2 | 3 | 0 | 0 | 0 | 3 | 0 | 0 |
| extramedullary hematopoiesis | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 1 | 4 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 3 | 0 | 0 |
| engorgement of erythrocyte | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 3 | 0 | 0 |
| liver | <5> | | | | <5> | | | | <5> | | | | <5> | | | | <5> | | | | <3> | | | |
| necrosis:single cell | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| hepatocellular hypertrophy:central | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 3 | 0 | 0 |
| kidney | <5> | | | | <5> | | | | <5> | | | | <5> | | | | <5> | | | | <3> | | | |
| papillary necrosis | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |

Grade 1: Slight 2 : Moderate 3 : Marked 4 :Severe
< > : Number of animals examined at the site