

Table 17.1 Effect of phenformin on life span and spontaneous carcinogenesis in female C3H/Sn mice.^a

Parameters	Control	Phenformin	$\Delta\%$; p
Number of mice	30	24	
Life span, days: Mean	450 \pm 23.4	545 \pm 39.2	+21.1%, $p < 0.05$
Last 10% of survivors	631 \pm 11.4	810 \pm 0	+28.4%, $p < 0.05$
Maximum	643	810	+26.0%
Aging rate $\alpha \times 10^3$, days ⁻¹	7.64 (7.59; 8.10)	5.26 (4.94; 5.51)	$p < 0.05$
MRDT, days	90.7 (85.6; 92.5)	131.8 (125.8; 140.3)	$p < 0.05$
Number of tumor-free mice	6 (20%)	19 (79.2%)	$p < 0.05$
Mean life span of tumor-free mice	362 \pm 49.0	557 \pm 41.6	+53.9%, $p < 0.05$
Number of tumor-bearing mice (TBM)	24 (80%)	5 (20.8%)	-3.8 fold, $p < 0.05$
Mean life span of TBM, days	472 \pm 25.1	499 \pm 111.6	+5.7%
Total number of tumors	41	5	
Number of tumors per TBM	1.7	1.0	-41.2%
Number of mice with mammary adenocarcinomas (MAC)	19 (63.3%)	4 (16.0%)	-4.0 fold, $p < 0.05$
Number of mice with leukemia	5 (16.7%)	1 (4.2%)	-4.0 fold, $p < 0.05$

^aLife spans are given as means \pm standard errors; 95% confidence limits are given in parentheses; MRDT = mortality rate doubling time.

with metformin. Treatment with metformin has been accompanied by a slow down of the age-related increase in blood glucose levels, as well as by a reduction in the levels of insulin, triglycerides and lipoproteins in the blood serum, compared with controls.²⁴

In experiments on female SHR mice, administration of metformin in a dose of 100 mg kg⁻¹ started at the age of 2 months shifted survival curve to the right, and increased mean life span by 38%.²⁵ In another experiment, the same strain of mice were given metformin in drinking water from the age of 3, 9 or 15 months.¹⁸ The mean life span of mice given the drug started at the age of 3 months increased by 14%, and the maximum one increased by 1 month. If treatment was started at the age of 9 months, the mean life span increased by only 6%, while in the older group it was not changed. The average life expectancy of mice without tumors increased by 21% and 7% in young and middle-age groups, respectively, whereas in old group it was decreased by 13%. It is important to note that in all age groups the use of metformin was accompanied by a decrease in the body temperature of mice and postponed age-related switching of the estrous cycle. The accumulation of senescent cells was slowed down in primary cultures of skin fibroblasts derived from mice injected with metformin from the age of 3, 9 or 15 months.³³

In inbred 129/Sv mice, the mean life span of males treated with metformin started at the age of 3 months was reduced by 13.4% in males and slightly