

Table 17.4 List of rodent strains used in studies on preventive effect of antidiabetic biguanides on carcinogenesis.

Species	Strain
Mice	A/J; <i>Apc</i> ^{Min/+} ; Balb/c; B6C3F1; CD1; C3H/S n; C57BL/6; C57BL/6(HBxTg); db/db; FVB/N; FVB/N-Tg; HBx; ICR; KPC; LID; LSA ⁺ L-Kras; trp53; p48Cre ⁺ . LSL-ras G12D; Swiss; Swiss H; outbred; PTEN ^{+/-} ; SHR; SOD1 ^{G92A} ; Swiss; Swiss-H; 129/Sv; Thrb ^{PV/PV} Pten ^{+/-}
Rats	F344; LIO; Sprague-Dawley; Wistar
Hamsters	Not shown

Table 17.5 Effect of antidiabetic biguanides on spontaneous and induced carcinogenesis in various organs and tissues in rodents.

No.	Target organ/tissue	Number of studies		
		Total	Positive effect	No effect
1.	Mammary gland	19	13	6
2.	Pituitary	2	2	0
3.	Thyroid gland	3	3	0
4.	Skin	3	3	0
5.	Soft tissues	2	2	0
6.	Uterus	5	5	0
7.	Cervix utery	1	1	0
8.	Lungs	4	4	0
9.	Oral mucosa	1	1	0
10.	Pancreas	4	4	0
11.	Pancreatic islets	1	1	0
12.	Liver	7	6	1
13.	Small interstines	3	1	2
14.	Colon	11	8	3
15.	Kidney	2	2	0
16.	Lymphoid tissues	5	4	1
17.	Nervous tissues	2	2	0
18.	Total tumor incidence	11	5	6
	Total studies	86	67 (77.9%)	19 (22.1%)

published.²⁶ Furthermore, only one study was focused on tumorigenesis in mice neonatally exposed to metformin. A detailed analysis of the experimental studies on anti-carcinogenic effect of antidiabetic biguanides has been done recently.^{22,23,40}

The biguanides suppressed tumor growth in the majority of *in vitro* studies conducted in 46 different cell lines originated from malignant tumors of 15 localization as well as in athymic mice with xenografts of 31 tumor lines.⁴⁰ It was concluded that there is sufficient experimental evidence of the anti-carcinogenic and antitumor effects of antidiabetic biguanides in a number of models of induced and spontaneous carcinogenesis.^{23,40} There are several hundred excellent reviews and meta-analyses of epidemiological data on the effect of metformin on cancer risk in type 2 diabetes patients(see, *e.g.*, ref. 10,41–45).