acid A by i.p. administration at a daily dose of 1.25–5 mg/kg for 5 days was reported. Growth of mouse sarcoma-37 cells were found to be completely inhibited by incubation with aristolochic acid A. Treatment of mice with aristolochic acid A at a daily i.p. dose of 2.5–5 mg/kg for 3 days after s.c. implantation of sarcoma-37 cells resulted in 40%–50% inhibition of tumor growth [50].

Aristolochic acid A, administered orally, reduced the number of tumors induced by methylcholanthrene in mice. The antitumor effect by oral administration was better than by parenteral injection [52]. Sex differences in both toxicity and antitumor activity of aristolochic acid A in mice with Ehrlich ascites carcinomas were also noted: Acute toxicity of aristolochic acid A was higher in males, whereas females were more affected by chronic administration. At a dose below the ED_{50} (1.15 mg/kg), aristolochic acid A had higher antitumor activity in males than in females; at higher doses the reverse was observed [53].

Aristolochic acid analogues and derivatives such as α-nitro-stilbene, β-nitrostyrene, and 1-(2-nitro-2-phenylvinyl)-naphthalene were synthesized and their cytotoxicity and antitumor activity were studied. The substituted nitrovinyl function of the latter compound was postulated to participate in a Michael type reaction with cellular nucleophilic groups [54], a reaction that was regarded to be relevant for cytotoxic activity.

Aristolochic acid A increased oxygen consumption in a dose dependent manner in liver cells and splenocytes of mice [55]. The metabolic activity of guinea pig peritoneal macrophages and human leukocytes was also enhanced by aristolochic acid A, as shown by measuring oxygen consumption [56].

Aristolochic acid A and aristolochic acid II exhibited a stimulation of lucigenin-enhanced, opsonized zymosan-induced neutrophil chemoluminescence as a sensitive assay for immunostimulating activity [57]. In a leukocyte adherence inhibition test, an activity of aristolochic acid A could also be demonstrated; however, it was weaker than that of prednisolone [58]. Following the administration of aristolochic acid A to guinea pigs immunized with Q fever antigen, the antigen-induced decrease in bone marrow lymphocyte count was restored to normal levels much faster than was observed in untreated immunized controls. Following Q fever immunization in rabbits, the antibody titer did not differ between treated and control animals, but a significantly higher antibody titer was observed in immunized rabbits treated with aristolochic acid A and prednisolone [59].

In contrast to the results described above, Xing et al. [60] reported that aristolochic acid A did not prolong the survival time of tumor bearing mice, enhance the immune function of the mouse reticuloendothelial system, or the phagocytic activity of mouse peritoneal macrophages.

Studies on acute toxicity showed LD_{50} values of 14.3 mg/kg, i.p., and 48 mg/kg, orally, in mice [61].

No apparent abnormalities in various organs were observed in rats after i.p. injection of ≤ 4 mg/kg daily for 7 days [61].

Mutagenic and carcinogenic activities of aristolochic acids were extensively studied. Aristolochic acid A was proven to be a direct mutagen in *Salmonella typhimurium* strains TA 1537 and TA 100. The presence of S9 mix had only a minor enhancing effect on the number of induced revertants. Aristolochic acid A had no mutagenic effect on TA 1535, TA 1538, or TA 98 with or without S9 mix [62]. Aristolochic acid II had almost equal mutagenic potency [63].