1 Animal Studies

1.1 Published

Bauer et al. (1977) administered freshly brewed standard commercial regular ground coffee (5.2 g/100 ml water) to C57BL/6J mice to provide a dose of approximately 120 mg/kg body weight/day. Standard rodent chow was fed ad libitum. One study involved 25 males in the coffee test group and 25 control males (receiving only water), a second study involved 27 animals in the coffee test group and 25 controls. The animals were kept on experiment for over 130 weeks in the case of the second test group. Gross and microscopic examinations were conducted on a wide variety of tissues and no unusual occurrence of tumors or cancer was found.

Macklin and Szot (1980) fed caffeine in the diet to male and female C57BL/6 mice. A total of 106 males and females received 55 mg/kg/day alone or in combination with phenacetin and aspirin for 75–80 weeks. On postmortem examination there were no remarkable findings that could be attributed to administration of these agents. Detailed histological examination of bladder, kidney and liver did not reveal any carcinogenic effect of the test chemical. The authors concluded that no evidence of carcinogenesis was demonstrated for any of the drugs, alone or in combination.

Wurzner et al. (1977) incorporated regular and decaffeinated instant coffees at a 6% level into a commercial standard diet. The coffee samples, extracted at different rates, were obtained from regular and decaffeinated coffees which were either freeze- or spray-dried. Outbred, specific-pathogen-free Sprague-Dawley rats were randomly distributed into 14 groups, each with 40 males and 40 females. A total of 240 males and 240 females received regular coffee and 120 males and 120 females received decaffeinated coffee with caffeine added. After experimental periods of 3 and 12 months, ten rats of each sex were chosen randomly from each group for interim examinations. The study was terminated at 24 months. Detailed gross and microscopic examinations were conducted on all animals. The authors concluded that “the data from our 2 year feeding study of regular and decaffeinated coffees in rats, using maximum tolerated dose levels, indicate no increased risk formation for neoplasms, and treatments providing high caffeine levels even decreased the evidence of neoplasm in both males and females”.

Zeitlin (1972) administered instant coffee solids to male and female Sprague-Dawley rats at a concentration of 5.0% in the diet from the weanling stage to 2 years
of age. The coffee content of the diet was 3.6%, providing a dietary concentration of 0.18% caffeine. Necropsies and histopathological examinations were conducted on all animals that died during the study and in survivors killed after 2 years. Particular attention was paid to the urinary bladder, which failed to show any evidence of abnormalities.

In a recent study in male Sprague-Dawley rats that was concerned with the potential carcinogenicity of analgesics, caffeine was included in one of the experimental diets at a level of 0.102% (Johansson 1981). Thirty rats were treated for 117 weeks, each receiving a total dose of 21.4 g caffeine. Control rats received the diet alone. The mean survival time for rats receiving caffeine was 78 weeks, with a range of 41–107 weeks. For control animals mean survival was 94 weeks, with a range of 67–116 weeks. There was no significant difference in the incidence of tumors between control and caffeine-treated animals. A total of six tumors were seen in control animals and eight in the caffeine group, all of types known to occur spontaneously in this strain of rat. The results of this study lend further support to the evidence that chronic exposure to very high doses of caffeine is without carcinogenic effect in laboratory animals.

Takayama and Kubawara (1982) reported a long-term study on the effect of caffeine in rats. Wistar rats of both sexes were given synthetic caffeine in their drinking water continuously for 78 weeks. Three hundred rats were divided into three groups of 50 males and 50 females each. Group 1 was given normal tap water without caffeine as a control, group 2 received 0.1% caffeine solution and group 3 was given 0.2% caffeine solution for 78 weeks. All the animals were killed after 104 weeks. Various tumors were found in both experimental and control groups, but their incidences were not higher in the experimental groups.

1.2 Unpublished

The results of unpublished studies are consistent with those of published studies; the findings after long-term administration uniformly indicate an absence of carcinogenic action.

Ito (1978) administered caffeine to groups of 50 ICR mice of each sex at levels of 0.2%, 0.1%, 0.05% or 0% in the drinking water. Male mice were killed after 60 weeks on test and females after 104 weeks. Gross and histological examinations were conducted on all organs. The incidence of neoplastic change was not significantly different in experimental animals and controls. The males were terminated prematurely on this study because of problems associated with fighting. The author concluded that this study provided no evidence for carcinogenic activity of caffeine.

In a National Cancer Institute study (1978), a mixture of aspirin, phenacetin and caffeine (APC) was administered in the feed at either of two concentrations to Fisher 344 rats and B6C3F1 mice. The high dose used in the chronic studies for the male and female rats and mice was 1.4% and the low dose was 0.7%. Fifty males and 49 or 50 females of each species were put on test materials and 50 animals of each sex were used as controls. After a 78 weeks of administration, observation of the rats continued for up to an additional 35 weeks and observation of the mice continued for an additional 16 weeks. No significant association was established be-