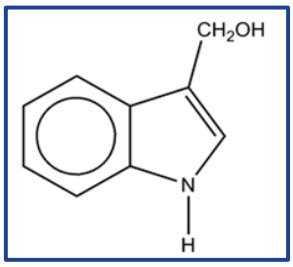
SUMMARY

Background: Indole-3-carbinol is naturally formed during the consumption of a variety of vegetables, such as broccoli, brussels sprouts, cauliflower, cabbage, kale, kohlrabi, and turnips. Indole-3-carbinol is also marketed as a dietary supplement for its potential ability to prevent cancer and provide other health benefits, such as detoxifying the liver and boosting the immune system. Exposure occurs through ingestion of these vegetables or dietary supplements. Although no overt toxicity has been reported in humans after the ingestion of indole-3-carbinol, the effects of oral administration of indole-3-carbinol in rats and mice were studied to identify potential toxicity or cancer-related outcomes.



Methods: Groups of 50 male and 50 female rats were orally administered 75, 150, or 300 milligrams (mg) of indole-3-carbinol per kilogram (kg) of body weight in corn oil, and groups of 50 male and 50 female mice were orally administered 62.5, 125, or 250 mg/kg. Control animals received 0 mg/kg (corn oil alone). Animals were administered indole-3-carbinol 5 days per week for 2 years. Additional 3-month studies were conducted to set appropriate doses and identify target organs for subsequent studies. Tests were conducted to evaluate the potential for indole-3-carbinol to cause DNA damage. At the end of the study, tissues from more than 40 sites from every animal were examined for signs of disease.

Results: The uterus was the primary site of carcinogenicity in female rats administered indole-3-carbinol. There was also an increase in the occurrence of skin neoplasms (which can include benign or malignant growths) in female rats administered the highest dose of indole-3-carbinol. In addition to these neoplasms, noncancerous tissue abnormalities were observed in the endometrium (tissue that lines the uterus) of female rats, the small intestines, mesenteric (membrane that attaches the intestine to the abdominal wall) lymph nodes, and liver in male and female rats, and in the thyroid gland of male rats. The liver was the primary site of carcinogenicity in male mice administered indole-3-carbinol—increases in liver neoplasms were primarily observed in male mice administered 125 or 250 mg/kg. A variety of noncancerous tissue abnormalities was also observed in the liver, glandular stomach (a tissue that secretes gastric acid), and nose of male and female mice. Tests to evaluate the potential for indole-3-carbinol to damage DNA produced inconclusive results.

Conclusions: *The NTP four-point scale rates the level of evidence that a substance has the ability to cause cancer in laboratory animals. Under the conditions of these 2-year gavage studies, there was clear evidence that indole-3-carbinol administration has the ability to cause liver cancer in male mice, some evidence that it has the ability to cause uterine cancer in female rats, equivocal (uncertain) evidence that it has the ability to cause skin cancer in female rats, and no evidence that it has the ability to cause cancer in male rats or female mice. In addition, indole-3-carbinol administration caused increased incidences of noncancerous tissue abnormalities in the small intestine, mesenteric lymph node, and liver of male and female rats; the thyroid gland of male rats; the uterus of female rats; and the liver, glandular stomach, and nose of male and female mice.*