Risco de câncer e bromo (bromatos)

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Etiology of bromate-induced cancer and possible modes of action-studies in Japan

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Renal cell tumors were significantly increased in male and female rats given potassium bromate at 250 and 500 mg/L in drinking water.
In at least one other study renal cell tumors were produced in male rats at 125 mg/L. Among male mice given 750 mg/L of potassium bromate, there were no significant differences in renal cell tumors between treated and control groups after 88 weeks on test. In oxidative DNA damage tests 8-oxodeoxyguanosine (8-oxodG also referred to as 8-OH-dG) was induced in DNA in the male rat kidney in 1 week, and in females after 3 weeks at 500 mg/L, and also in both male and female rats at 250 mg/L, but not at 125 mg/L. DNA adducts are considered to be an initial step in the carcinogenesis process, however, the administered doses are not always sufficient to cause mutations, possibly due to DNA repair. In the two-step rat renal carcinogenesis model using N-ethyl-N-hydroxyethylnitrosamine (EHEN) as initiator, promotion activity by potassium bromate was measured using the BrdU labeling index. The promoting activity of bromate in male rats was much greater and extended to doses as low as 60 mg/L in male rats, whereas in females the response was limited to 250 and 500 mg/L. Therefore, it was concluded that the mechanisms contributing to cancer in the male rat were more complex than in the female rat. The accumulation of alpha2mu-globulin in the kidneys of male rats exposed to potassium bromate probably accounts for the greater labeling index in the male rat relative to the female rat. Accumulation of alpha(2mu)-globulin as a result of treatment with chemicals is unique to the male rat and does contribute to carcinogenic responses. Neither humans nor female rats display this response. Nevertheless, bromate must be considered carcinogenic because of the response of the female rats. The better correlation between 8-oxodG formation and tumor response indicates that dose-response information from the female rat would be much more relevant to human risk assessment. The fact that an elevation of BrdU-LI in the kidney of the female rat is consistent with the possibility that cell proliferation observed in female rats resulted from oxidative stress and/or cytotoxic responses in the kidney. Therefore, oxidative stress is most likely the mechanism of interest for cancer risk in humans.

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Toxicity and carcinogenicity of potassium bromate--a new renal carcinogen.

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Potassium bromate (KBrO3) is an oxidizing agent that has been used as a food additive, mainly in the bread-making process. Although adverse effects are not evident in animals fed bread-based diets made from flour treated with KBrO3, the agent is carcinogenic in rats and nephrotoxic in both man and experimental animals when given orally. It has been demonstrated that KBrO3 induces renal cell tumors, mesotheliomas of the peritoneum, and follicular cell tumors of the thyroid. In addition, experiments aimed at elucidating the mode of carcinogenic action have revealed that KBrO3 is a complete carcinogen, possessing both initiating and promoting activities for rat renal tumorigenesis. However, the potential seems to be weak in mice and hamsters. In contrast to its weak mutagenic activity in microbial assays, KBrO3 showed relatively strong potential inducing chromosome aberrations both in vitro and in vivo. Glutathione and cysteine degrade KBrO3 in vitro; in turn, the KBrO3 has inhibitory effects on inducing lipid peroxidation in the rat kidney. Active oxygen radicals generated from KBrO3 were implicated in its toxic and carcinogenic effects, especially because KBrO3 produced 8-hydroxydeoxyguanosine in the rat kidney. A wide range of data from applications of various analytical methods are now available for risk assessment purposes.

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