

A combined chronic toxicity/carcinogenicity study of sucralose in Sprague-Dawley rats.

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The chronic toxicity and potential carcinogenicity of sucralose was evaluated by exposing Sprague-Dawley rats to dietary concentrations of this low-calorie sweetener both in utero and for up to 104 weeks following parturition. The rats assigned to the toxicity phase of this investigation were administered diets containing either 0% (control), 0.3% (3000 ppm), 1.0% (10,000 ppm) or 3.0% (30,000 ppm) sucralose.

Each treatment group comprised 30 male and 30 female rats, of which 15 males and 15 females were sacrificed after 52 weeks of treatment. The surviving rats were killed following 78 weeks of sucralose administration. In the carcinogenicity phase of this investigation, groups of 50 male and 50 female rats were administered dietary sucralose at concentrations of 0% (control 1), 0% (control 2), 0.3%, 1.0% or 3.0% for 104 weeks. Evaluation of the data obtained from the two phases of this study showed that sucralose was not carcinogenic.

Sucralose did not adversely affect the survival or clinical condition of the rats, and there were no toxicologically significant findings. Group mean body weight gain and food consumption were significantly decreased in a dose-dependent manner in sucralosetreated rats throughout the treatment period as compared to the controls. The primary effect of sucralose on food consumption, and secondarily on body weight gain, was established in later studies to be due to the fact that diets containing high concentrations of sucralose are unpalatable to rats.

These subsequent studies established that the reduction of body weight gain seen in previous rat studies using sucralose in the diet at concentrations of 1% and below resulted from reduced food intake as a direct consequence of the unpalatable nature of sucralose. Similarly, at concentrations of 3% in the diet, it was shown that approximately 95% of the effect on body weight gain could be attributed to the reduction in food intake due to the



reduced palatability of the diet, the remainder apparently due to a physiologic response to the high concentrations of non-digestible sucralose in the rats' diet.

Complete toxicological evaluations of gavage studies with histopathological evaluations demonstrated that even at the 3% dietary level, toxicity was not responsible for the small body weight gain decrement. Gross and histopathologic examinations revealed that the administration of sucralose affected neither the types nor incidence of the tumours observed.

The incidences of some nonneoplastic findings were statistically significantly increased in the sucralose treated groups relative to the controls. These included: renal pelvic epithelial hyperplasia in all female treatment groups, renal pelvic mineralization in females administered the intermediate or highest dietary concentrations of sucralose, adrenal cortical haemorrhagic degeneration in high-dose group female rats, and the histopathologic incidence of cataracts at necropsy in high-dose group male rats.

The non-neoplastic findings that occurred were of no toxicological significance since they were either spontaneous findings commonly observed in aged rats of this strain or the physiological response to high dietary levels of a poorly absorbed compound.