PERGAMON

Food and Chemical Toxicology 38 (2000) 773–781

Food and Chemical Toxicology

www.elsevier.com/locate/foodchemtox

Research Section

Studies on the carcinogenicity of potassium iodide in F344 rats

K. TAKEGAWA, K. MITSUMORI *, H. ONODERA, T. SHIMO, K. KITAURA, K. YASUHARA, M. HIROSE and M. TAKAHASHI

Division of Pathology, National Institute of Health Sciences, 1-18-1 Kamiyoga, Setagaya-ku, Tokyo 158-8501, Japan

(Accepted 15 February 2000)

Abstract—A chronic toxicity and carcinogenicity study, in which male and female F344/DuCrj rats were given potassium iodide (KI) in the drinking water at concentrations of 0, 10, 100 or 1000 ppm for 104 weeks, and a two-stage carcinogenicity study of application at 0 or 1000 ppm for 83 weeks following a single injection of *N*-bis(2-hydroxypropyl)nitrosamine (DHPN), were conducted. In the former, squamous cell carcinomas were induced in the salivary glands of the 1000 ppm group, but no tumors were observed in the thyroid. In the two-stage carcinogenicity study, thyroidal weights and the incidence of thyroid tumors derived from the follicular epithelium were significantly increased in the DHPN + KI as compared with the DHPN alone group. The results of our studies suggest that excess KI has a thyroid tumor-promoting effect, but KI per se does not induce thyroid tumors in rats. In the salivary gland, KI was suggested to have carcinogenic potential via an epigenetic mechanism, only active at a high dose. *© 2000 Elsevier Science Ltd. All rights reserved*

Keywords: thyroid; salivary gland; *N*-bis(2-hydroxypropyl)nitrosamine.

Abbreviations: DHPN = *N*-bis(2-hydroxypropyl)nitrosamine; Hb = hemoglobin; HE = hematoxylin-eosin; Ht = hematocrit; KI = potassium iodide; PLT = platelet counts; RBC = red blood cell counts; SCC = squamous cell carcinoma; SPF = specific pathogen free; WBC = white blood cell counts.

INTRODUCTION

Potassium iodide (KI) has been used as a food additive for iodine supplementation in iodine deficient regions, for therapy of goitre and for patients experiencing difficulty in expectoration caused by asthma. It is well known that iodine deficiency exerts promoting effects on thyroid neoplasia in the rat (Capen, 1996; Collins and Capen, 1980; Ohshima and Ward, 1986). In a two-stage carcinogenicity model, in which rats are first administered with *N*-bis(2-hydroxypropyl)nitrosamine (DHPN), a genotoxic carcinogen for the thyroid, thyroidal proliferative lesions such as nodular hyperplasia or adenoma were induced by iodine-deficiency (Kanno *et al*., 1992). On the other hand, excess KI administration at a concentration of 260 ppm in the drinking water has been reported to also promote thyroid carcinogenesis in rats initially treated with DHPN (Kanno *et al*., 1992). However, there is no experimental study to investigate whether KI *per se* has thyroid carcinogenic potential. KI has not been reported to have any mutagenicity, but may have effects via epigenetic events. When excess iodine is given to rats, as an acute response, the serum T4 level decreases and TSH production is stimulated. However, no acute morphological changes are observed in follicular epithelia in the thyroid (Wolf *et al*., 1949). Chronic administration results in the histological appearance of so-called colloid goitre, with follicular dilatation accompanied by flattened epithelia, although serum TSH levels are more normal (Correa and Welsh, 1960; Kanno *et al*., 1992; Wolff, 1969). Many iodinated compounds have been reported to inhibit 5′-deiodinase and to possibly also promote thyroid tumor via serum TSH increase in response to a drop in circulating T3 (Laurberg and Boye, 1987; Ruiz and Ingbar, 1983).

The present study was conducted to determine whether KI alone can cause thyroidal tumors with long-term application for 2 yr. In addition, the effects

*Corresponding author. Tel: +81-3-3700-9845; fax: +81-3-3700-1425; e-mail: mitsumor@nihs.go.jp

0278-6915/00/$ - see front matter © 2000 Elsevier Science Ltd. All rights reserved. Printed in Great Britain
PII: S0278-6915(00)00068-5