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Some toxic effects of boric acid on rats

B. T. Lim*

Key words: toxicity, boric acid

Abstrak

Asid borik diberi kepada tikus selepas dicampurkan dengan makanan kawalan. Sukatan yang diberikan ialah 0.30–0.35 g/kg berat badan sehari. Bulu tikus banyak gugur selepas diberi asid borik selama 4 bulan. Antara bulan ketiga dan bulan ke-10 tikus yang diberi asid borik kurang makan berbanding dengan tikus kawalan. Antara bulan keempat dan bulan ke-10 berat badan tikus yang diberi asid borik juga kurang daripada berat badan tikus kawalan. Tiada tanda pembentukan sel kanser pada organ tikus ujian dan tikus kawalan selepas 6 bulan percubaan dijalankan.

Abstract

Boric acid was given to rats by incorporating it in the diet. The dosage of boric acid given was 0.30–0.35 g/kg body weight per day. Rats suffered from an abnormal hair loss after receiving boric acid for 4 months. Between the third month and the 10th month, the average feed intake of both the male and female rats receiving boric acid was significantly lower ($p < 0.05$) compared with that of the control rats. During the fourth month and the 10th month, the body weight of rats receiving boric acid were significantly lighter ($p < 0.05$) compared with that of the control rats. There was no sign of cell lesion in the various organs examined after 6 months of exposure to boric acid.

Introduction

The use of boric acid as food preservatives dates back to the 1850s when it was first used in Italy. It was later used in many countries for preserving a variety of foods such as margarine, butter, liquid rennet, liquid egg-yolk and caviar. The concentrations of boric acid used range from 0.5% to 1.0%. Boric acid has now been widely prohibited as food additive in many countries, including Malaysia. However, it is still being used in many types of locally processed foods such as noodles, fish balls, 'fucuk' and salted fish (Normah and Ku Hasnah 1985).

Boric acid is a weak acid with a very low dissociation constant. The solubility of boric acid is about 5 g in 100 mL of water at room temperature. It is present in an almost undissociated and microbiologically effective form, even in the neutral pH range where other preservatives are unsatisfactory (Leuck 1980). Boric acid is therefore superior in preserving neutral foods, except that comparatively higher concentrations need to be used. The use of boric acid is mainly against yeast. Its inhibitory effect against moulds and bacteria is only very slight (Leuck 1980).

*Food Technoogy Division, MARDI, P.O. Box 12301, 50774 Kuala Lumpur, Malaysia
Author's full name: Lim Bon Tong
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Boric acid is rapidly and completely absorbed by the body and excreted only very slowly (Pfeiffer et al. 1945). If taken over a longer period through food, an accumulation of boric acid in the body is therefore likely. It is generally accepted that boric acid is poisonous when taken in large amounts. General symptoms of acute poisoning include severe diarrhoea, vomiting, abdominal pain, nausea, visual disturbances, coma and convulsions (Goldbloom and Goldbloom 1953). The LD_{50} of boric acid on rats was reported to be 2.66 g/kg body weight per day by Pfeiffer et al (1945), and 5.14 g/kg body weight per day by Windholz et al. (1983). There has been no conclusive study on the chronic toxicity of boric acid.

Chronic toxicity tests are frequently performed by exposing rats or mice for 1–2 years (Anon. 1978). The main purpose of conducting chronic toxicity tests is to find the toxic effects which are manisfested only after prolonged exposure. An important investigation is to assess the carcinogenic potential. The results obtained can be used to predict possible human risk. For chronic toxicity tests, the highest dose possible should be chosen so that definite toxicity is apparent, yet does not materially decrease the life span of the test animals.

Materials and methods

Boric acid powder (H_3BO_3) from MERCK was used throughout the experiment. The animals used were white rats obtained from the Institute of Medical Research, Kuala Lumpur.

Groups of 30 male and 30 female rats (approximately 6 weeks old) were housed individually in cages kept in air-conditioned animal house. They were first placed on a control diet formulated for laboratory animals for 1 week. For the treatment, 15 control animals of each sex received only the control diet while the remainder animals received boric acid admixed to the diet. Boric acid was fed to the rats at 0.30–0.35 g/kg body weight per day. The dosage level was controlled by determining the feed intake and body weight. The dosage used was equivalent to 11–13% of LD_{50} reported by Pfeiffer et al. (1945), and 6–7% of LD_{50} reported by Windholz et al. (1983). Control diet was formulated as in *Appendix 1*, *Appendix 2* and *Appendix 3* (Anon. 1975). The daily appearance and behaviour of all animals were visually observed at noon. Feed intake and body weights were also recorded daily.

At every 6-month interval, one-third of the total number of rats were sacrificed for histological examination. The organs examined include kidney, pancreas, liver, intestines and stomach. Fresh tissues were fixed in Bouin's solution, sectioned by using a microtome knife, mounted on slides, stained and examined microscopically for signs of cell lesion or tumour formation.

The experiment was conducted as a completely randomized design (Steel and Torrie 1980). Analysis of variance was carried out for each test of significance.

Results and discussions

Rats after receiving boric acid for 4 months showed abnormal loss of hair compared with the control animals (*Table 1*). This has resulted in patches of hair loss on the body of the rat. During the third month and the 10th month, the average feed intake of both the male and female rats given boric acid was

Table 1. The physical appearance and behaviour of rats exposed to boric acid

Duration (month)	Treated rats	Control rats
1– 4	Normal	Normal
5– 8	Patches of hair loss	Normal
9–12	Patches of hair loss	
	Less active	Normal

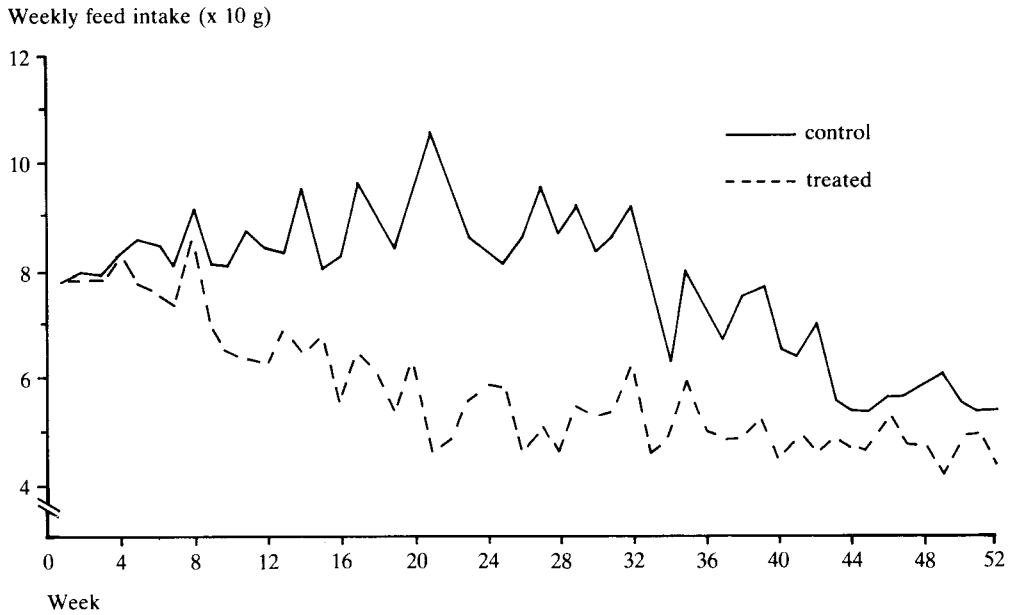

Figure 1. Weekly average feed intake per male rat

Table 2. Number of unexpected deaths recorded

Month	Treated rats		Control rats	
	Male	Female	Male	Female
1	0	0	0	0
2	0	0	0	0
3	0	0	0	0
4	0	0	0	0
5	0	0	0	1
6	1	0	1	0
7	0	1	0	1
8	1	1	0	1
9	1	1	1	1
10	1	1	2	0
11	3	1	1	2
12	2	3	3	2
Total	9	8	8	8

significantly lower ($p < 0.05$) compared with that of the control rats (*Figure 1* and *Figure 2*). Therefore, ingestion of boric acid has decreased the overall feed intake of rats. Between the fourth month and the 10th month, the body weights of both male and female rats receiving boric acid were significantly lighter ($p < 0.05$) when compared with the body weight of control rats (*Figure 3*). However, the differences among the males seem to be more evident than the females.

There was no sign of lesion or tumour formation in the organs of both the control and treated rats after the first 6 months. After 7–8 months of experiment, the mortality rate of both control and treated rats increased due to unexpected death (*Table 2*). The cause of the unexpected death was unknown. As a result, the remaining rats were sacrificed after 12 months of study. Histological examination of the tissues of the remaining rats also showed no sign of lesion or tumour formation. However, the number of rats survived at the 12th month was too small for any valid conclusion on histological examination.

The results obtained showed that prolonged ingestion of boric acid was harmful for the growth of rats. The

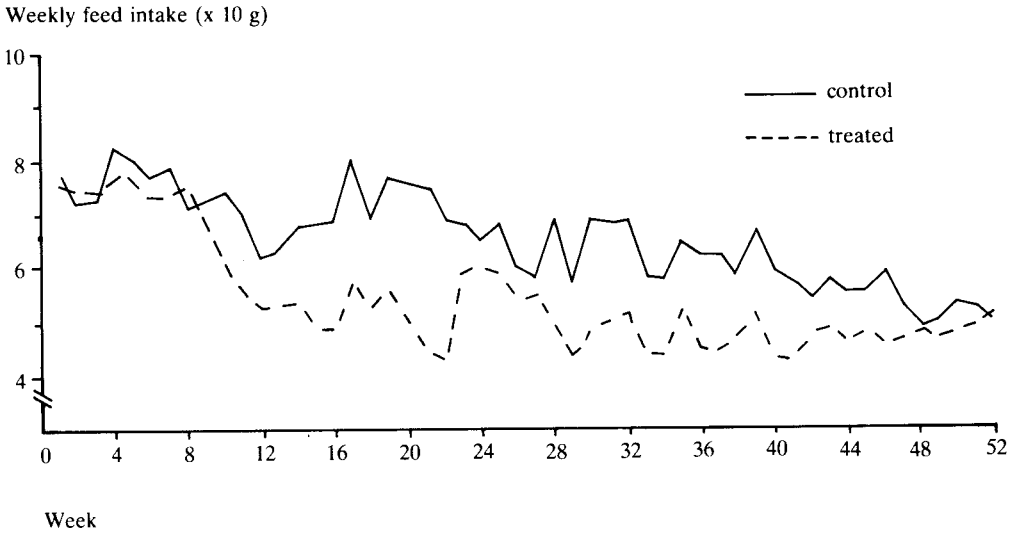

Figure 2. Weekly average feed intake per female rat

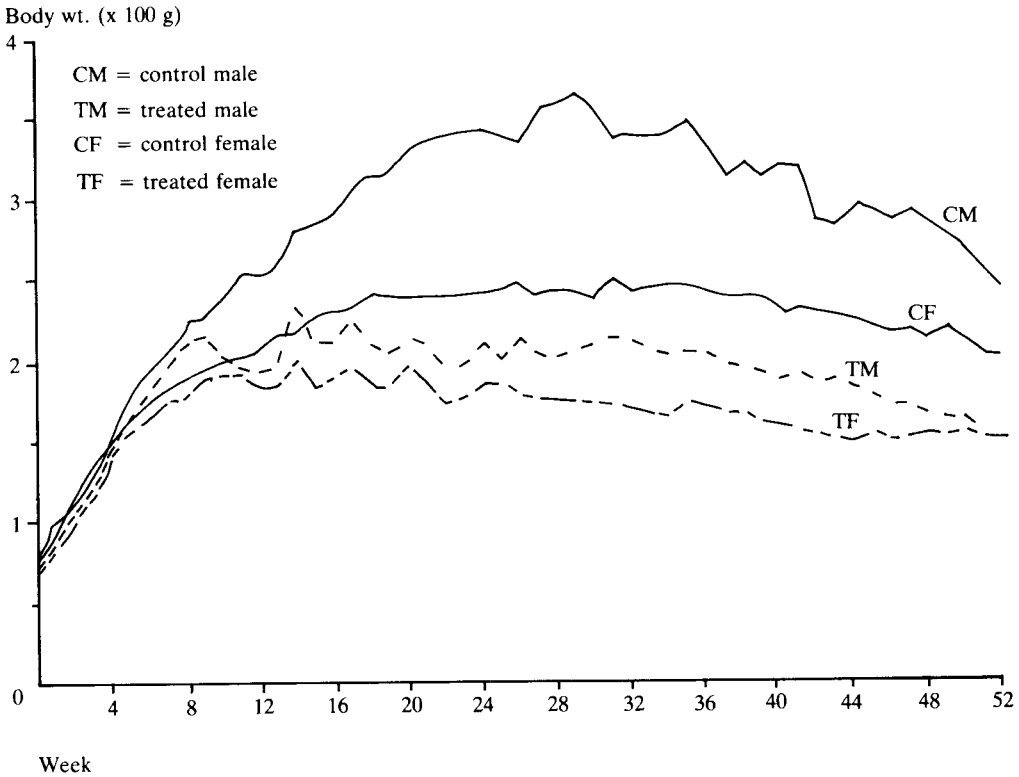

Figure 3. Weekly average body weight per rat

decrease in feed intake of rats receiving boric acid was unlikely to be due to gastrointestinal tract irritation, as saturated aqueous solution of boric acid has been reported to be nonirritating (Snell and Snell 1962). These observations will be useful to those who intend to conduct further toxicological testing on boric acid.

Conclusion

Rats after receiving boric acid in the diet at 0.30–0.35 g/kg body weight per day for 4 months suffered from abnormal hair loss. Between the third month and the 10th month, the feed intake of both male and female rats receiving boric acid was significantly lower ($p < 0.05$) than that of the control rats. During the fourth month and the 10th month, the body weights of both the male and female rats were also significantly lower ($p < 0.05$) than that of the control rats. There was no sign of cell lesion in the kidney, pancreas, liver, intestines and stomach at the sixth month of exposure.

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Appendix 1. Composition of control diet for rats

Ingredient	% of diet
Casein	12.13
Glucose	10.00
Vitamin mixture	1.00
Mineral mixture	5.00
Corn oil	5.00
Corn flour	66.87
Total	100.00

Appendix 2. Composition of vitamin mixture

Vitamin	mg/g of mixture
Vitamin A	2 000 (IU)
Vitamin D	200 (IU)
Vitamin D_2	10 (IU)
Menadione	0.5
Choline	200.0
p-aminobenzoic acid	10.0
Inositol	10.0
Niacin	4.0
Ca *D*-panthothenate	4.0
Riboflavin	0.8
Thiamine, HCL	0.5
Pyridoxine, HCL	0.5
Folic acid	0.2
Biotin	0.04
Vitamin B_{12}	0.003
Glucose, enough to make 1 000 mg	

Appendix 3. Composition of mineral mixture

Mineral	g/kg of mixture
Sodium chloride	139.30
Potassium iodide	0.79
Potassium dihydrogen orthophosphate	389.00
Magnesium sulphate anhydrous	57.30
Calcium carbonate	381.40
Ferrous sulphate	27.00
Zinc sulphate	0.55
Cupric sulphate	0.48
Cobaltous chloride	0.02
Manganous sulphate monohydrate	4.01
Total	1 000