a = 63.014, b = 52.909, and ED_{50}, 0.568. On the same figure are plotted the results obtained previously in the same laboratory. The ED_{50} which produced a 50% antagonism of the pancuronium-depressed twitch tension were 18, 49, 440, and 600 $\mu g\ kg^{-1}$ for neostigmine, pyridostigmine, 4-aminopyridine, and galanthamine respectively. Galanthamine provoked a 10-25% increase of systolic blood pressure in 34 (80%) of the animals. The effect lasted from 3 to 19 min. Onset time to peak effect with galanthamine was similar to that seen by Miller et al[7] with neostigmine, both of them exerting a more rapid onset than that of pyridostigmine and 4-aminopyridine. Duration of galanthamine antagonism was similar to that of neostigmine and pyridostigmine, but shorter than that of 4-aminopyridine.

On the basis of the study, and comparing the results with those of Miller and his colleagues[7], galanthamine is the least potent of the 3 cholinesterase inhibitors. Its potency is rather similar to that of 4-aminopyridine (fig.). However, the validity of this comparison might well be disputed on 2 points. Firstly, the log dose response curve for galanthamine was constructed around 5 points whereas those of the other compounds were on 3 points. Secondly, in our hands, unlike Miller et al., it was impossible to maintain the steady state of the deep pancuronium block before galanthamine administration for more than 8-10 min, whereas Miller et al. waited 15 min. The rise in blood pressure seen here could well have been prevented had atropine been given[8]. The anticholinergic agent was not injected because of reports stating that the muscarinic side effects of galanthamine are minimal[9].

In conclusion, a constant infusion of a non-depolarizing neuromuscular drug in the rat tibialis anterior-sciatic nerve preparation is a useful agent in comparing and assessing antagonists to muscle relaxants. Galanthamine was about 30 times weaker than neostigmine and this is in good agreement with the 1:18 ratio observed on the phrenic nerve preparation[4] and the ratio of 1:20 seen in human studies[3].

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Toxicity of Temik (aldicarb) for a fresh water teleost, *Barbus conchonius* Hamilton

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Summary. The toxic effects of Temik (aldicarb) on a fresh water Himalyan lake teleost, *Barbus conchonius* were investigated in hard and soft water. The 48-, 72- and 96-h TL_m-values in mg/l were 8.99, 2.39 and 2.42 respectively in the hard-water test and 3.30, 0.62 and 0.46 in the soft-water test. The toxicity of Temik to *B. conchonius* increases many fold in soft water.

The use of carbamates for the control of agricultural pests is a common practice, although it is well known that they are a source of aquatic pollution, hazardous for the life of piscine and non-piscine fauna. The literature hitherto available deals with the detrimental effects of carbamates such as carbaryl and mexacarbate[2,3]. Temik, a newer systemic pesticide belonging to the carbamate group, is in use to control agricultural pests[4]. It has been found to be toxic to beneficial insects[5] and birds[6], too. However, there is no information on the toxicity of Temik to fishes. On account of its high solubility in water (6000 ppm), Temik is liable to be washed into bodies of water. The present report deals with the acute toxic limits of Temik for a Himalyan lake teleost, *Barbus conchonius*, in hard and soft water; to the best of our knowledge it is the first on this subject.

Healthy specimens of *B. conchonius* (4.8 ± 0.45 cm in size), collected from the high altitude Himalyan lake Nainital, were acclimatized to laboratory conditions for at least 1 week in a quality of water similar to that in which the toxicity bioassays were carried out. During the acclimatisation, fishes were fed rice bran. The hardness in terms of $CaCo_3$ and pH of the water was 318.57 ± 1.6 and 7.41 in the case of hard water and 60.69 ± 0.15 and 7.16 in the case of soft water. The temperature variation during the period of experiments was between 14 and 22 °C. The bioassay experiments were performed in stationary water by exposing the fishes to various concentrations of Temik; between 0.25 ppm and 1.50 ppm for the soft-water test and 1.00 ppm and 6.00 ppm for the hard-water test. There was no food supply during the course of the experiment.

The mortality data collected at 28, 72 and 96 h were analyzed for the calculation of TL_m-values according to the procedure of Finney[7]. The comparative TL_m-values of Temik for *Barbus conchonius* in hard and soft water are

Comparative TL_m-values of Temik for *B. conchonius* in hard and soft water

Time (h)	Hard water No. of test animals	TL_m-values ± SE (mg/l)	95% confidence limits (mg/l)	Soft water No. of test animals	TL_m-values ± SE (mg/l)	95% confidence limits (mg/l)
96	180	2.42 ± 0.010	2.28–2.52	210	0.459 ± 0.0010	0.445–0.521
72	180	2.39 ± 0.011	2.18–3.951	210	0.623 ± 0.0012	0.492–2.692
48	180	8.99 ± 0.014	4.265–18.586	210	3.296 ± 0.0017	1.116–9.727

given in the table. The median tolerance limits obtained for various periods clearly indicate that Temik is a potent toxicant for *B. conchonius*. The concentrations of 1.5 ppm in soft water and 6.00 ppm in hard water resulted in 100% mortality within 96 h. As is already known for other pesticides, the toxicity of Temik increases many fold in softer water. The present short term experiments were also capable of producing histopathological changes in important organs like gills, liver and kidney, which probably account for the lethal effects of this pesticide.

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Zinc, copper and manganese levels in various tissues following fluoride administration

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Summary. Distribution of zinc, copper and manganese has been studied in liver, kidney and bone of rats subjected for 10 months to varied fluoride concentrations in drinking-water. In the liver a significant fall in the levels of Mn, Cu and Zn was registered. In the kidney, the Mn level fell whereas the zinc level increased. In the bone, the copper content fell, whereas the manganese content increased.

Fluoride is now widely advocated as an effective means of reducing the incidence of dental caries. However, inorganic fluoride, when excessively ingested, is toxic. Further, fluoride is known to interact with and alter the metabolism of calcium[1,2], magnesium[3,4] and iron[5]. The object of the present communication is to report the effect of fluoride administration on some other essential metallic nutrients like zinc, copper and manganese.

Material and methods. Female albino rats (Wistar strain), obtained from the Central Research Institute, Kasauli (India) were used in the present study. 24 animals, each weighing 125–170 g, were segregated into 3 groups of 8 animals each and were subjected for 10 months to varied fluoride concentrations in the drinking water, viz. 0 ppm: control; 10 ppm (10 mg/l): group I; 25 ppm (25 mg/l): group II. The animals were fed ad libitum with a balanced pellet feed, supplemented with requisite amounts of trace elements.

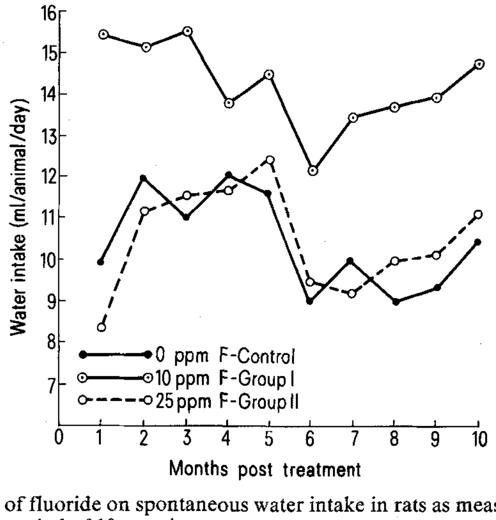
After the treatment, the animals were sacrificed and their liver, kidneys and bone (femur) removed. The tissues were then processed according to Barker et al.[6] for analysis by atomic absorption spectrophotometer. In brief, the processing involved sequential treatment of a known amount of dried tissue with nitric acid and perchloric acid, followed by appropriate dilution with deionized water. The statistical significance of the data on Zn, Mn and Cu was evaluated by Student's t-test.

Results. The data pertaining to water intake are shown in the figure. The rats of group II (25 ppm F) exhibited a much higher water intake than the controls. The fluoride treatment did not have a significant effect on the growth of the animals as evidenced by monthly gain in body weight. The growth curves of control and experimental animals were almost identical, and are therefore not shown in a figure.

There was a significant decrease in the zinc levels of bone and liver in group II, 13% and 29%, respectively. However, the kidneys in group II showed an increase of 34% in the zinc content. The copper concentration in the liver fell by 21% in group II. No significant change was observed in the copper concentration in the kidneys of either experimental group. Depletion of copper in the bone was very pronounced; it was 41% in group II. The manganese levels in group II also fell by 24% and 26% in the liver and kidney respectively whereas this element increased by 38% in the bone in the same group.

During the course of the present study, no significant alterations were observed in the tissue levels of zinc, copper and managnese in group I (10 ppm). It may be mentioned here that the recommended concentration of fluoride in the drinking-water for the prevention of dental caries varies from 0.7 to 1.5 ppm (0.7–1.5 mg/l) depending upon the climate which in turn affects the total water intake[7].

Discussion. The zinc depletion observed in the liver and bone following fluoride ingestion is known to have an adverse effect on metalloenzymes[8], which are vital for



Effect of fluoride on spontaneous water intake in rats as measured over a period of 10 months.