The influence of ingested fluoride on the ascorbic acid concentration in guinea-pig tissues

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Summary. Fluoride added to drinking water at concentrations of 50 and 70 ppm provided highly significant increases in the ascorbic acid concentration in tissues but was without effect on the serum alkaline phosphatase and cholesterol.

Although fluoride is a potent in vitro inhibitor of enzyme systems there is little evidence that even substantial increases in the fluoride intake modify enzyme activity in vivo[2,3]. Ascorbic acid is a labile component of most tissues and previous studies have indicated that decreases in its tissue concentration might act as a sensitive indicator of physiological and metabolic stress[4-6]. A number of basic experiments were designed, primarily to determine whether a high dietary fluoride intake modified tissue ascorbic acid in this way.

Methods. Male albino Dunkin-Hartley guinea-pigs were given a semi-synthetic scorbutogenic diet previously described but with fluoride omitted from the salt mixture[4,5]. All the guinea-pigs received a daily maintenance dose of ascorbic acid administered orally. 4 experiments were done; in each experiment a group given drinking water containing fluoride (as sodium fluoride) was compared with a non-fluoride group. The structure of the experiments is indicated in the table. In experiments 1, 2 and 4 3-month-old guinea-pigs were used and in experiment 3 9-month-old ones. B.w. changes and food and water intake were recorded daily. Experiment 1 continued for 15 days and experiments 2, 3 and 4 for 25 days. At the end of the experiments the guinea-pigs were killed by decapitation, blood collected, organs removed and weighed and the serum alkaline phosphatase (experiment 1), serum cholesterol (experiments 1 and 2) and tissue ascorbic acid (experiments 1, 2, 3 and 4) determined as in previous studies[7].

Results and discussion. There were no fluoride induced changes in the serum cholesterol and serum alkaline phosphatase (2 labile blood components of fairly widespread metabolic significance) nor in the absolute and relative organ weights. In experiment 1 the fluoride supplement (70 ppm) produced a growth depression attributable in part to an initial reduction in fluid intake: this did not occur when the fluoride content of the drinking water was reduced to 50 ppm or less (experiment 2, 3, 4). In all experiments there were greater ascorbic acid concentrations in the tissues of fluoride - treated animals than in those of the controls (table). Drinking water with 16, 8 and 4 ppm fluoride produced no significant increase of tissue ascorbic acid: of possible relevance in this respect is the report that only at levels greater than 30 ppm could fluoride modify the intracellular potassium of cultured cells[8].

The concentrations of fluoride used in this experiment were considerably greater than those normally considered acceptable for supplementation purposes - although Messer, Armstrong and Singer have reported that pregnant mice given a 50 ppm supplement in drinking water had a significantly better reproductive record than low fluoride mothers and that the haematocrits of the '50 ppm offspring' were greater than those of the 'low-fluoride' group[3].

Our results point to a clearly definable metabolic effect of fluoride outside the usual areas of fluoride involvement (dental and skeletal structure). A possible explanation is that fluoride inhibits tissue enzymes involved in the breakdown of ascorbic acid[9,10]. There are recent indications that breakdown products of ascorbic acid may have mutagenic properties[11]; this could be of some significance in any somatic mutation theory of ageing. Of interest in this context are observations that the life span of *Drosophila* is decreased by ascorbic acid and that of mice prolonged by a dietary fluoride supplement[12,13].

Influence of dietary fluoride on tissue ascorbic acid concentrations in guinea-pigs

Experiment	Ascorbic acid intake (mg/100 g b.w. daily)	Fluoride in water (ppm)	Ascorbic acid (mg/100 g) Adrenals	Spleen	Liver	Brain
1 (6)	0.5	0	26.8±2.1	9.71±1.01	4.91±0.61	7.92±0.51
1 (7)	0.5	70	37.0±2.2*	12.17±1.14*	5.30±0.5	8.24±0.43
2 (7)	0.5	0	27.2±2.3	9.96±0.83	3.81±0.32	6.91±0.40
2 (7)	0.5	50	97.3±5.9**	31.1±1.6**	11.6±0.6**	17.9±0.61**
3 (6)	0.2	0	3.30±0.91	1.84±0.26	2.06±0.16	2.26±0.23
3 (8)	0.2	50	8.39±1.09**	3.72±0.36**	2.44±0.19**	3.54±0.26**
4 (6)	0.5	0	34.2±2.9	12.2±0.23	3.93±0.26	8.89±0.27
4 (5)	0.5	32	39.5±3.4	12.3±1.00	4.72±0.44	10.16±0.58*

Means with SE; the figures in brackets are the number of animals in each group at the end of the experiment.
*Difference between means for the group $p < 0.05$; **$p < 0.01$.

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