Urol Res (1985) 13:175–178

**Urological Research**



# Fluoridation of Drinking Water: Effects on Kidney Stone Formation

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Accepted: September 25, 1985

**Summary.** The influence of fluoride in drinking water on stone formation was studied in animals and in "in vitro" cristallization experiments. In male Wistar rats fluoride inhibits ethylenglycol induced calcification of the kidneys and stone formation. The in vitro results performed in synthetic urine exhibited a dose-dependent delay of cristal growth.

**Key words:** Fluoride in drinking water, Kidney calcification, Synthetic urine, Stone formation.

**Table 1.** Trial of animal experiment – different admixture to drinking water

| | fluoride | ethyleneglycol | *n* |
|---|---|---|---|
| A | – | – | 10 |
| B | 10 ppm | – | 20 |
| C | 10 ppm | 0.8 p.c. | 20 |
| D | – | 0.8 p.c. | 20 |

## Introduction

In 1976 Luoma and coworkers [1] described an animal experiment in which fluoride intake in low dose could prevent induced nephrocalcinosis. On the other hand Anasuya [2] generated calciumoxalate stones in animals by high calcium/high fluoride diet (23 mg fluorine/kg diet) while in a low fluoride diet less stones were formed. Ljunghall [3] and Summers [4] reported higher stone incidence in regions with drinking water fluoridation. Investigations of Müller, Hesse and Schneider [5] showed higher fluoride excretion in urine and higher fluoride contents in calcium oxalate stones produced by fluoridation of drinking water.

Fluoridation of Drinking water has been practised in Basel since 1962, providing the means to investigate the influence of fluoride in drinking water on calcium oxalate stone forming in animals and in vitro experiments.

## Materials and Methods

### *A) Animal Experiment*

The growth of calcium oxalate stones in 200–300 g male Wistar rats was induced by ethylenglycol in the drinking water. Ethylenglykol will be metabolized endogenous to oxalate [6]. 4 different groups were investigated (Table 1).

The rats were fed with commercially available rat fodder (NAFAG, fluorine content 6.7 ppm).

During two different periods 8 h-urine was collected under metabolic ward conditions. Urinary calcium, sodium, potassium and fluoride were determined. Of each group half the animals were killed after 20 days, the others after 60 days and kidneys and femura resected. The analysis of the cations was made by flame atomic absorption spectrometry (FAAS), that of fluoride by a Metrohm fluoride-sensitive electrode. The kidneys were wet mineralized, concentrations correspond to dry weight.

### *B) In Vitro Studies*

A synthetic urine inorganic and organic main components of which correspond to a so-called normal human urine was used.

To 10 ml of synthetic urine with different fluoride concentrations (1, 5, 10 ppm $F^-$) 39 mmol sodium oxalate were added and the kinetic of precipitate formation determined. To avoid a nucleation caused by friction no magnetic stirrer could be used. Instead of that the solution was agitated mechanically with constant frequency and amplitude at 37 °C. After 2 and 4 min respectively the formed calcium oxalate crystals were separated by filtration over a fritted glass crucible P-4 (pore diameter 9–15 $\mu$). The crystals which remained on the crucible were washed with iced water, dissolved in warm hydrochloric acid and the calcium content determined by FAAS.

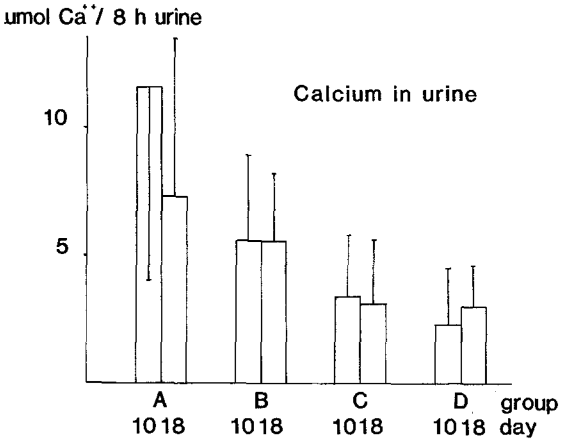


Fig. 1. Calcium excretion in urine. Animal experiment: *A*, control group; *B*, fluoride supplement; *C*, fluoride and ethylenglykol supplements; *D*, ethylenglykol supplement, different times of trial

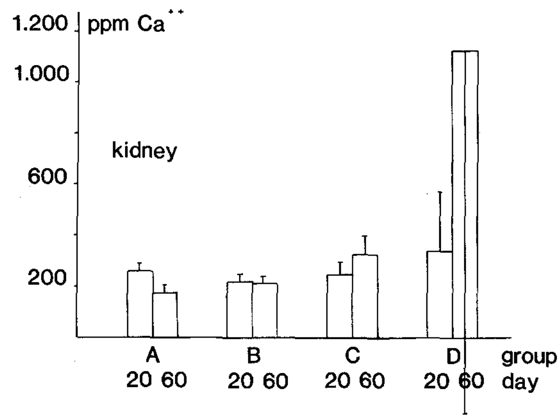


Fig. 3. Calcium content of kidneys – animal experiment at different times

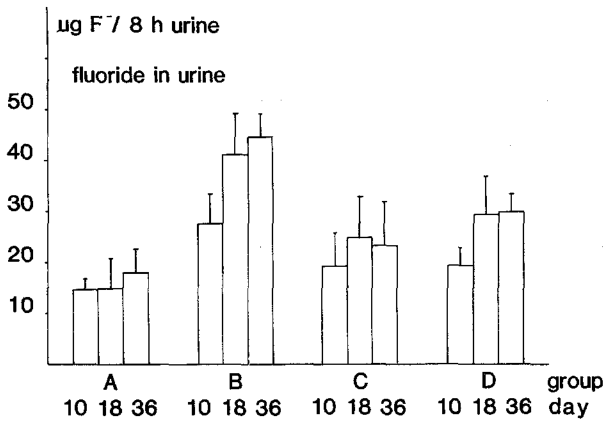


Fig. 2. Fluoride excretion in urine – animal experiment at different times

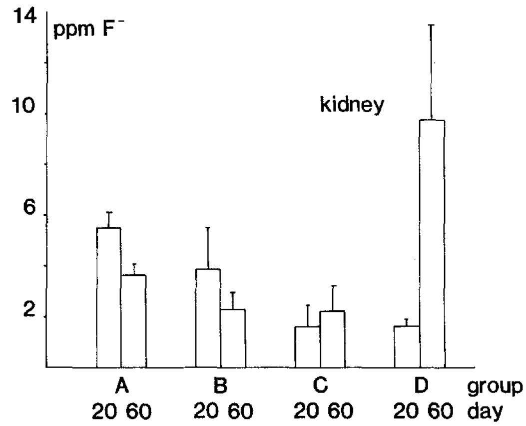


Fig. 4. Fluoride content of kidneys – animal experiment at different times

## Results

### *A) Animal Experiment*

*Calcium Excretion in Urine (Fig. 1).* Calcium excretion was studied on the 10th and 18th day of the experiment. Group A showed obviously higher calcium excretion compared to the groups treated with fluoride and/or ethylenglykol. The lowest values could be seen in group D (only ethylenglykol). Significant differences between the 10th and 18th day were not observed.

*Fluoride Excretion in Urine (Fig. 2).* Fluoride excretion was studied on the 10th, 18th and 36th day. Urinary fluoride excretion of group A remained constant. In group B (only fluoride) an increase on the 18th day and an unchanged excretion on the 36th day was determined. However, group C and D showed lower but relatively constant values compared with group B.

*Calcium Content of Kidneys (Fig. 3).* In group A, B and C no remarkable differences in calcium content could be seen. Compared with those groups kidneys of group D rats (killed the 60th day) showed obviously higher calcium content. These observations are also correlated with striped calcerous deposits in those kidneys. Two of these ten rats had stones.

*Fluoride Content of Kidneys (Fig. 4).* Highest fluoride concentrations were also found in the kidneys of group D. It is striking that group C and D (rats killed the 20th day) have lower fluoride values than the other groups.

*Fluoride Content of Femura.* Between the groups no significant differences could be observed. Furthermore no effects were seen in dependence on experimental period.

*Sodium and Potassium Excretion in Urine.* Also in this case no differences between the groups and during the experimental period could be observed.

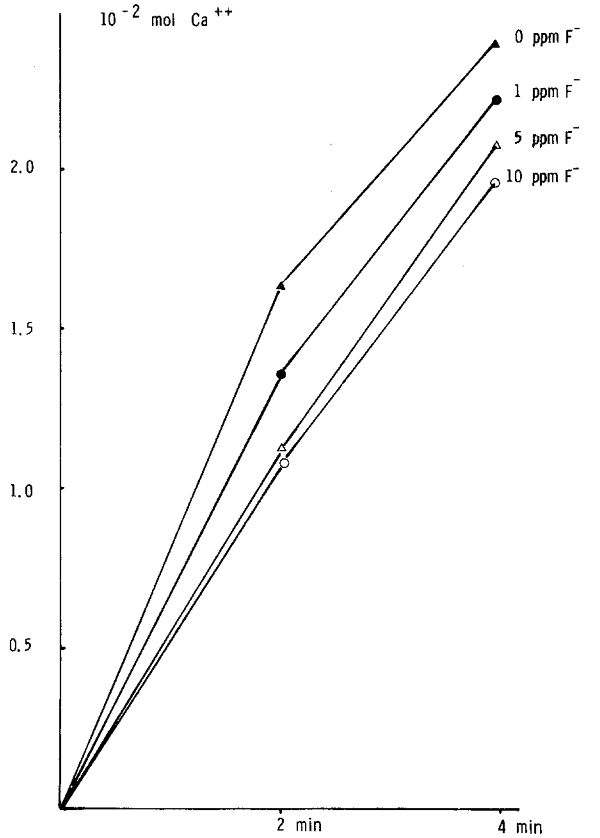


**Fig. 5.** Dependence of crystal growth versus fluoride content and time

**Table 2.** Dependence of crystal growth versus fluoride content and time

| fluoride content | 2 min p.c. | 4 min p.c. |
|---|---|---|
| 0 ppm | 100 | 100 |
| 1 ppm | 72 ± 10 | 89 ± 11 |
| 5 ppm | 64 ± 9 | 85 ± 8 |
| 10 ppm | 56 ± 19 | 81 ± 15 |

*B) Measuring of Cristallization in Synthetic Urine (Fig. 5/Table 2)*

To determine the influence of fluoride on crystallization kinetic of calcium oxalate it is vital to use solutions of constant and reproducible composition at constant temperature and under controlled precipitation conditions. The synthetic urine corresponds to human urine in terms of ionic strength and main components. The concentrations of the single components are taken in regard of the mean concentrations of human urine [7].

In our investigations fluoride delays crystal growth and thus the mass of filterable calcium. Figure 5 reflects the mass of crystallized calcium versus time and fluoride concentration. Compared to synthetic urine without fluoride (= 100%) only 72% of the crystals precipitate after 2 min at a fluoride presence at 1 ppm, 64% at 5 ppm and 56% at 10 ppm. After 4 min these differences are levelled. Based on studies at pH 5.3 and 6.1 no pH-dependence could be observed in this range.

## Discussion

In 1956 Spira proposed a dependence of drinking water fluoridation in increased stone disease [8]. Summers and Keitzer [4] pointed out a correlation between increasing calcium oxalate stone disease and initiated fluoride prophylaxis. On the other hand Hermann and Papadakis [9] and Luoma, Nuuja, Collan and Nuumikoski [1] could not confirm these results by animal experiment. Without doubt calcium oxalate stones contain more fluoride in regions with fluoride prophylaxis [8, 10, 11, 12, 13].

The effect of fluoride on stone formation is ill understood. Meyer and Nancollas [14] observed a dual mechanism in in vitro studies. Their paper suggested that low concentrations of fluoride depress, and high concentrations promote the growth of calcium phosphate. This agrees with the animal experiments of Anasuya [2], who proposed a heterogenous nucleation caused by fluoride.

Our in vitro studies point out a dose-dependent inhibitor mechanism. Increasing fluoride concentrations (0, 1, 5, 10 ppm) effected an inhibition of crystal growth. Our measurement equipment allows the determination of crystals bigger than 9 $\mu$. The observed effects are detectable only within a period of 4 min.

These results agree with the data obtained in the animal experiment. Finlayson and Reid [15] calculated an intrarenal passage time of about 2–3 min. In our opinion predominantly small crystals are formed during this short period in presence of fluoride and then swept out with the urine. Growth of bigger crystals starts in the bladder or in the voided urine but could not be determined in our animal experiment.

In conclusion we assume that crystal growth relevant to stone formation is delayed by fluoride.

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