Fluoride in the oral environment

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A predominant part of the cariostatic activity of fluoride is a function of its concentration in the fluid environment of the teeth. The fluoride exposure results in a slightly elevated steady-state level of fluoride in the oral fluids, primarily in saliva and plaque fluid. So far, however, little is known about the intra-oral fluoride concentration necessary to achieve a cariostatic effect at the site of action. Following fluoride intake, the fluoride remaining in the oral cavity is diluted by the saliva pool. The remaining fluoride may be found in several compartments in the oral cavity. It may be ionized in saliva, ionized in plaque (plaque fluid), bound in plaque, bound as calcium fluoride, bound to enamel, and bound to soft tissues. Fluoride is also distributed to the oral tissues and into the dental plaque by diffusion. It is well established that plaque, after fluoride exposure, becomes a fluoride reservoir which stores for some time and releases fluoride. The present review gives an insight into the important parameters that determine the disposition and fate of fluoride in the oral environment. To achieve in-depth understanding, and hence formulation of the optimal fluoride therapy, more information is needed to consolidate our understanding of the distribution, retention, and elimination of fluoride in the oral cavity. Such knowledge will form a better basis for providing our patients with more effective dental fluoride products and regimens. □ *Caries; clearance; plaque; saliva*

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Nowadays, it is generally accepted that a predominant part of the cariostatic activity of fluoride is a function of its concentration in the fluid environment of the teeth. The most effective caries-preventive fluoride regimen, shown in a large number of clinical trials, is the frequent (daily) exposure of the oral cavity to low concentrations of fluoride, e.g. through fluoridated water or fluoridated toothpaste (1). The exposure to fluoride results in a slightly elevated steady-state level of fluoride in the oral fluids, primarily in saliva and plaque fluid. It is therefore reasonable to assume that a dose–response relationship should exist between the concentration of fluoride in these fluids and the cariostatic potential of a fluoride dental product. So far, however, little is known about the intra-oral fluoride concentration necessary to achieve a cariostatic effect at the site of action.

Following fluoride intake, the fluoride remaining in the oral cavity is diluted by the saliva pool. The fluoride left behind can be found in several compartments in the oral cavity. It may be ionized in saliva, ionized in plaque (plaque fluid), bound in plaque, bound as calcium fluoride, bound to enamel, or bound to soft tissues. Fluoride is also distributed to the oral tissues and into the dental plaque by diffusion. It is well established that plaque, after fluoride exposure, will become a reservoir storing fluoride for some time before releasing it. The fluoride released is adsorbed to or integrated in the mineral phases of teeth.

The purpose of this review is to give a brief survey of what is currently known about the disposition and fate of fluoride in the oral environment.

Normal salivary concentration

In subjects eating a normal diet and living in an area with about 0.2 ppm fluoride in the water supply, a number of studies have shown that the fluoride concentration in saliva is about 0.6 μmol/L (0.01 ppm) (2). However, this figure largely depends on the use of fluoridated toothpaste, other fluoride containing agents, and food items. The diurnal variation can thus be considerable (see Fig. 1) (3). For children living in areas with 1.2 ppm fluoride in the water supply, the salivary fluoride concentration has been shown to vary during the daytime between 0.5 and roughly 2.0 μmol/L (4). It may be concluded that for a given regimen of daily fluoride intake baseline fluoride in saliva is constant (2, 5). When a change in the fluoride intake regimen occurs, there will be a new steady state (6).

Factors influencing salivary clearance

The salivary fluoride concentration increases immediately after intake of a fluoride source. The increase and the profile of the fluoride concentration curve is determined by the release of fluoride from the vehicle and the fluoride content of the product. An additional factor that may also influence the concentration profile is the existence of flavoring agents in these products that stimulate the salivary flow, resulting in a faster dilution and thus elimination of the fluoride content of saliva (7). This overall process of fluoride elimination from the saliva pool

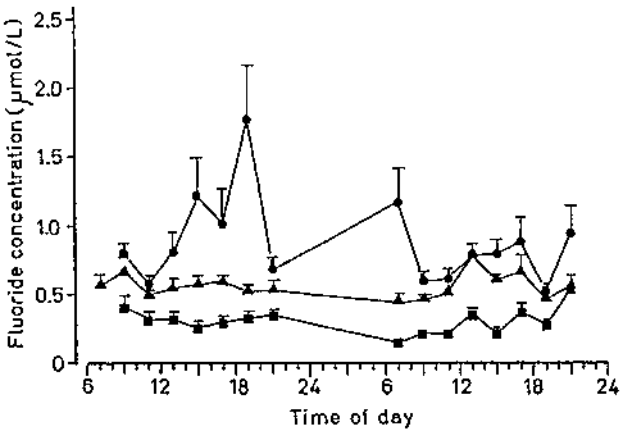

Fig. 1. Mean basal salivary fluoride concentrations during 2 consecutive days in subjects from 3 different fluoride areas (■) 5.3, (▲) 10.5, and (●) 63.2 µmol/L (0.1, 0.2, and 1.2 ppm) fluoride in the drinking water (3). Error bars denote 1 SE.

is termed salivary fluoride clearance. Based on Daves's (9) mathematical model of sugar clearance from the oral cavity, Lagerlöf & Oliveby (8) developed a theoretical model of the fluoride clearance process. The essential features of this model are shown in Fig. 2. The mouth is assumed to act as an incomplete siphon into which saliva flows at a rate determined by the stimulating action of any tastant in the mouth but with basal secretion rate equivalent to the unstimulated salivary flow rate. As saliva enters the mouth, the volume of saliva in the mouth increases until a swallow occurs. The volume is then reduced to a minimum level and the cycle starts again. The mean volume of saliva before swallowing has been established as 1.1 mL (range 0.5–2.1 mL) and the residual mean volume after swallowing is estimated at 0.8 mL (range 0.4–1.8 mL) (10).This model predicts that fluoride clearance takes longer in subjects with low unstimulated salivary flow rate than in those with high unstimulated flow rate.

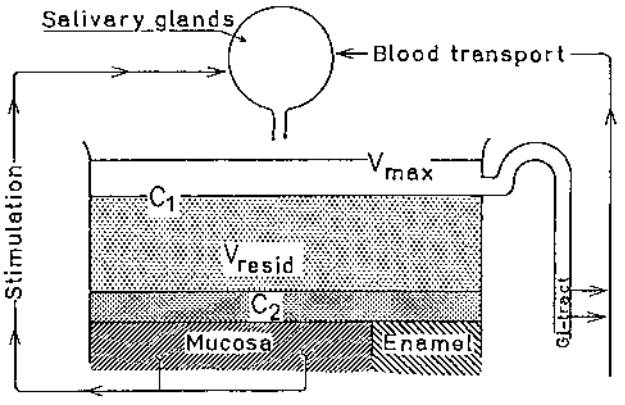

Fig. 2. Schematic model of salivary fluoride clearance. C_1 represents the saliva; C_2 represents the integuments and plaque on teeth and mucosa; $V_{resid}$is the volume of saliva after swallowing; V_{max} is the volume of saliva before swallowing (3).

In addition to the variation in salivary flow, there are other factors that determine the concentration of fluoride in saliva. Zero et al. (11) found that edentulous patients retain more fluoride after an application than dentate patients. It has also been shown that individuals with gingival recession retain higher fluoride levels than individuals without gingival recession (12).

Besides, the fluoride vehicle of topical application also influences the oral retention of fluoride. Zero et al. (12) demonstrated that a fluoride rinse was a more effective way of elevating oral fluoride concentration over time than fluoride dentifrice. Administration of lozenges gave a higher peak salivary fluoride concentration and a lower fluoride clearance rate than the same amount of fluoride administered as dentifrice via a toothbrush (13). No difference in the stimulation of salivary flow rate was found between these two vehicles.

Recycling of fluoride via salivary glands

Contrary to most electrolytes, the fluoride concentration in saliva is independent of salivary flow rate. In unstimulated and stimulated parotid saliva, submandibular/sublingual saliva, and whole saliva, the fluoride concentration is about 2/3 of the simultaneously collected plasma (14–17). This relationship is maintained when the plasma fluoride concentration is increased by fluoride ingestion. Thirty minutes after fluoride ingestion, the peak fluoride concentration in plasma is reached; this occurs a little later in saliva (15–17).

Absorption through the GI tract generates a small fraction of the total fluoride dose recycled into the oral cavity via the salivary glands. This was studied pharmacokinetically when 1 mg NaF was given as a gelatin capsule, i.e. no fluoride was released from the capsule in the mouth before swallowing. It was found that about 0.05% appeared in unstimulated whole saliva during the 2 h following ingestion (15).

Fluoride in plaque

Information on the dynamics and kinetics of fluoride in plaque usually refers only to the total fluoride in plaque. The fluoride concentration is reported to range from 1 to about 10 ppm (5, 18).

Much of the fluoride in plaque is held in complexes in dynamic equilibrium with the fluoride in the fluid phase of the plaque (19). Although a large number of studies have dealt with fluoride in plaque, most of them refer to fluoride in whole plaque.

In a recent study, changes in the fluoride concentration in saliva and plaque fluid at 6 single tooth sites were followed for up to 180 min after a rinse with a 0.048 mol/L fluoride solution of either NaF or MFP (sodium

monofluorophosphate) (20). The baseline level of fluoride in plaque fluid ranged from 15 to 17 μmol/L, which was about 30 times higher than the baseline value in saliva. The maximum fluoride concentration in saliva after the NaF rinse was on average 13 times higher than that of the MFP rinse. About 5% of the total amount of fluoride (18.2 mg F) following the 20 ml NaF rinse was retained in the oral cavity after expectoration. The corresponding figure following the MFP rinse was less than 1%. The saliva/plaque fluid fluoride ratios for upper molars and lower incisors were significantly higher than for the upper incisors and lower molars. There was also a tendency for a decline in the ratios with respect to time for all sites. The high concentration of fluoride in plaque fluid relative to saliva suggests the existence of large labile fluoride reservoirs in plaque.

Analysis of the decline in the plaque fluid fluoride concentration curves at various sites revealed an exponential decline in most cases (20). In the NaF rinse experiments, the baseline plaque fluid fluoride levels were not reached within 3 h. A bi-exponential pattern with a breakpoint at 90 min was apparent in all curves. A typical clearance curve from these studies is shown in Fig. 3. It was also clearly demonstrated that a NaF rinse resulted in a significantly higher intra-oral fluoride exposure in comparison with MFP solution of the same fluoride concentration. It therefore appears that most of the MFP is eliminated via salivary clearance before any notable hydrolysis occurs. Since NaF does not need a hydrolysis step to deliver fluoride, larger amounts of fluoride deposits, such as CaF_2 or cellular bound fluoride, may form in plaque.

The fluoride distribution and clearance from different sites of the oral cavity are apparently linked to salivary access to these sites (21–23). These site-specific differences may have clinical consequences with regard to the dynamics of fluoride in the demineralization and remineralization processes.

The most common sources of fluoride in toothpaste are MFP and NaF, and these compounds deliver fluoride to the oral cavity by different mechanisms. NaF is readily available in the oral fluids in contrast to MFP which needs a hydrolysis step to release fluoride. This hydrolysis step may be the major reason accounting for the observation that NaF toothpaste shows higher salivary (24) and plaque fluid fluoride concentrations than MFP toothpaste (5). This may also explain why there seems to be a stronger anticaries effect provided by a NaF toothpaste than by a MFP toothpaste (25, 26). Finally, preliminary studies on the kinetics of fluoride in plaque fluid following the exposure of the oral cavity to a slurry of NaF or a MFP toothpaste with the same fluoride content confirm the findings from the rinsing studies mentioned above.

The present review has only given an insight of the important parameters that determine the disposition and fate of fluoride in the oral environment. To achieve in-depth understanding and hence the formulation of the optimal fluoride therapy, more information is necessary of the distribution and retention in the oral cavity and elimination of fluoride from the oral cavity. Such knowledge will provide a better basis for treating our patients with more effective dental fluoride products and regimens.

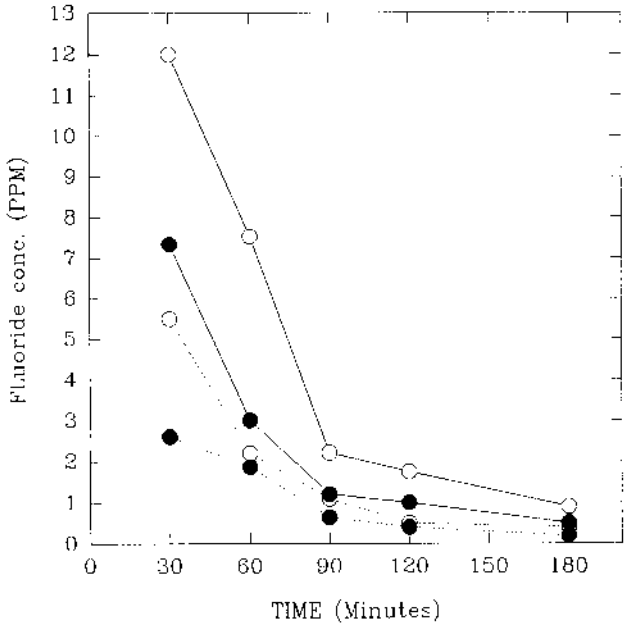

Fig. 3. Plaque fluid fluoride (solid line) and salivary fluoride (dotted line) after NaF (○) or MFP (●) rinse. The plaque was collected from upper and lower molars in one subject. Data from Ekstrand 1997 (20).

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