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Fluoride bioavailability in saliva using DENTTABS® compared to dentifrice

Research Article

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Abstract: It was the aim of this study to assess fluoride retained in saliva after use of fluoride-containing tablet DENTTABS® compared to toothpaste containing amine fluoride. Four subjects (2 normal saliva secretors, 1 slow secretor, and 1 fast secretor) participated in this crossover study comparing DENTTABS® and ELMEX®. After baseline sample collection, calibrated study personnel brushed the subjects' teeth with the assigned product for 3 minutes. Saliva samples were taken at baseline (T0), immediately after brushing (T1) and then 10 (T2), 25 (T3) and 85 (T4) minutes post-brushing. The amount of saliva collected was measured, and the fluoride content was analysed. All 4 subjects repeated all study cycles 5 times. Statistical analysis was done using the Mann-Whitney-U test and Spearman correlation. The fluoride retention was significantly higher after brushing with DENTTABS® at T1 and T2. There was a correlation between individual salivary flow rate and the F- content. Flow rate in g/min ranged from 1.1 to 3.8 at T1 and from 0.2 to 1.1 at T4 with much higher F- retention in slow secreting cycles. The saliva fluoride clearance kinetics of two equal amounts of fluoride-containing oral hygiene products demonstrate higher retention for DENTTABS®.

Keywords: *Fluoride • Saliva • Dentifrice • Oral hygiene tablets • Bioavailability*

1. Introduction

The bioavailability of fluoride (F) in the oral fluids plays a crucial role in inhibiting caries lesions because of the well established effect on the demineralisation/remineralisation process [1-3]. The kinetics of fluoride in saliva have been studied intensively comparing different F^- compounds in dentifrices [4], mouthrinses [5], fluoride chewing gum [6,7], fluoridated salt [8], fluoride tablets [9], and fluoridated milk [10]. These pioneering studies clearly demonstrated the significant elevation of fluoride concentrations in saliva after administration of topical formulations with rapid peaks and different kinetic behaviour of the salivary fluoride clearance.

It is the aim of preventive and curative treatment of incipient caries lesions via remineralisation of a biomineral deficit to provide a lifelong bioavailability of fluoride in the oral fluids. This was the reason for formulating a novel oral hygiene agent in tablet form (DENTTABS®, Prodentum, Berlin, Germany) aimed at properly removing plaque and stains, stimulating saliva secretion, polishing tooth surfaces with less abrasiveness and, most importantly, elevating fluoride concentration in oral fluids. The clinical efficiency of tooth brushing and plaque removal has been investigated, demonstrating the same results compared to a standard dentifrice [11], but the claim of bioavailability of fluoride from sodium fluoride has not been proven.

In contrast to the fluoride content solved in wet toothpastes or in liquid mouthwashes, the sodium fluoride in the tablets is solved exclusively in saliva as the most important medium for remineralisation. Variables of concentration are reduced to the individual saliva secretion rate, expectoration, and deglutition. The F^- concentration is independent from the mixing behaviour of dentifrice or mouthwash formulation in saliva.

It was, therefore, the aim of this investigation to assess the fluoride bioavailability in saliva after using DENTTABS® compared to the dentifrice ELMEX® and to correlate the fluoride clearance kinetics to the individual saliva secretion rate.

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Table 1. Mean fluoride content in saliva (ppm ±SD) before and after tooth brushing with 0.33 g DENTTABS® (4350 ppm) and 1g ELMEX® (1400 ppm) and designated follow-ups in 4 subjects.

Retention time	DENTTABS®		ELMEX®	
	Mean ± SD	Median; min/max	Mean ± SD	Median; min/max
T0 Baseline	0.19 ± 0.07	0.201; 0.06/0.23	0.19 ± 0.07	0.201; 0.06/0.23
T1 0 min	166.4 ± 75.9	165.2; 64.2/287.3	125.3 ± 44.7	123.7; 67.9/202
T2 10 min	19.1 ± 9.4	22.7; 2.7/27.5	14.2 ± 8.9	15.2; 1.9/30.3
T3 25 min	1.2 ± 0.9	0.96; 0.06/2.8	1,2 ± 1.0	1.3; 0.04/2.3
T4 85 min	0,05 ± 0.03	0.05; 0.004/0.1	0.06 ± 0.04	0.06; 0.01/0.1

The drinking water contained 0.1-0.3 ppm natural fluoride.

2. Experimental Procedures

2.1. Subjects

Four healthy test persons, comprised of 2 normal saliva secretors, 1 slow secretor and 1 fast secretor, participated in this crossover study (2 male and 2 female subjects, 43-65 years of age). They consented after verbal and written information on the aim and performance of the investigation and also received written instructions and a schedule. Participants were further asked to avoid fluoride-rich food products such as tea, fish and specified mineral water during the period, but had no restrictions concerning drinking water. All test subjects were residents in the area with ~0.2 ppm fluoride in the drinking water and normally used fluoride-containing dentifrices twice daily. The participants had good oral health.

2.2. Fluoride products

Oral hygiene tablets DENTTABS® (Prodentum GmbH, Berlin) contain 4350 ppm fluoride from NaF per 0.33 g tablet. The other ingredients according to INCI are microcrystalline hydroxyethylcellulose, hydrated silica, sodium hydrogen carbonate, sodium lauryl sulphate, ascorbic acid, magnesium stearate, aspartame and mint flavour. The pH is adjusted to 5.5.

The dentifrice ELMEX® (Gaba, Lörrach, Germany) contains 1400 ppm fluoride from Olaflur®. According to INCI the other ingredients are water, hydrated silica, hydroxyethylcellulose, sorbitol and saccharine, peppermint oil, menthol, anethole, spearmint oil, limonene and titanium dioxide adjusted to pH 4.6.

2.3. Study design

The study protocol was approved by the Ethical Committee of the University of Witten/Herdecke, Germany. After baseline sample collection (T0), calibrated study personnel brushed the subjects' teeth with the assigned product for 3 minutes. Saliva samples were taken immediately after brushing (T1) and at 10 (T2), 25 (T3) and 85 (T4) minute intervals post-brushing, each time collecting whole saliva for 10 minutes. The amount of saliva collected was weighted and the secretion rate determined and expressed as g/min. All subjects repeated the two study cycles five times, and the data of three cycles per subject for both fluoride formulations underwent statistical analysis.

2.4. Fluoride determination

After collection of whole saliva and weighting, the samples were centrifuged (Biofuge B Centrifuge, Beckman Instruments Inc., Krefeld, Germany) for 10 minutes at 6000 rpm in micro-centrifuge tubes. An aliquot of 1 ml was taken and mixed with 1 ml of a TISAB II buffer solution (Thermo Electron, Beverly, MA, USA). For fluoride ion distribution during the measurement, a magnetic stick stirrer (size 2x5 mm) was used. The salivary fluoride content was analysed using a fluoride-sensitive electrode (96-09 Orion, Thermo Electron, Beverly, MA, USA).

For measurement of the fluoride content the following analytical techniques were used: direct calibration and incremental techniques, the method of known addition for low ionic strength samples with a fluoride concentration of less then 0.38 ppm.

Direct calibration was performed in a series of prepared standards of 0.04, 0.4, 4.0, 40 and 400 ppm fluoride.

2.5. Statistical Methods

The obtained data were processed with the Statistical Package for Social Sciences (SPSS 15.0, Chicago, III., USA). The post-brushing values were compared with baseline levels using the Mann-Whitney-U test with ANOVA for repeated measures. Correlations were assessed with the Spearman coefficient. The level of significance was determined at $p<0.05$.

Figure 1. Fluoride content in unstimulated whole saliva from 4 test persons (1 fast saliva secretor (a), 2 normal secretors (b), and 1 slow secretor (c)) immediately after brushing (T1) with DENTTABS® and ELMEX®.

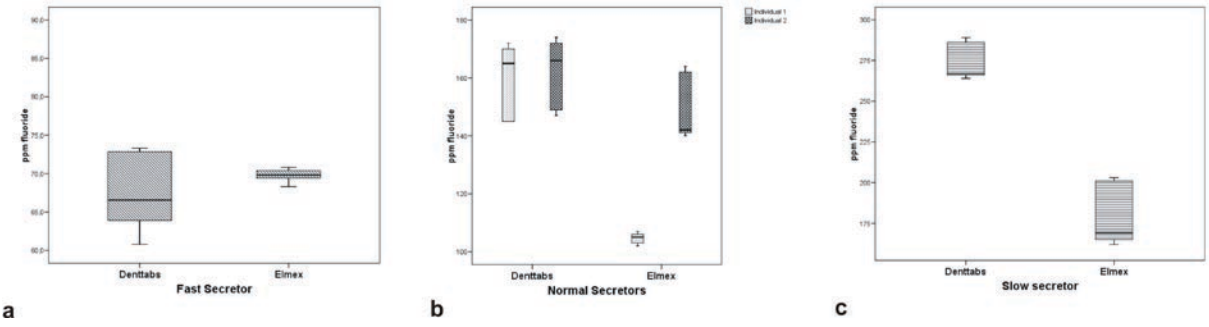


Figure 2. Fluoride content in unstimulated whole saliva from 4 test persons (1 fast saliva secretor (a), 2 normal secretors (b), and 1 slow secretor (c)) 10 minutes after brushing (T2) with DENTTABS® and ELMEX®.

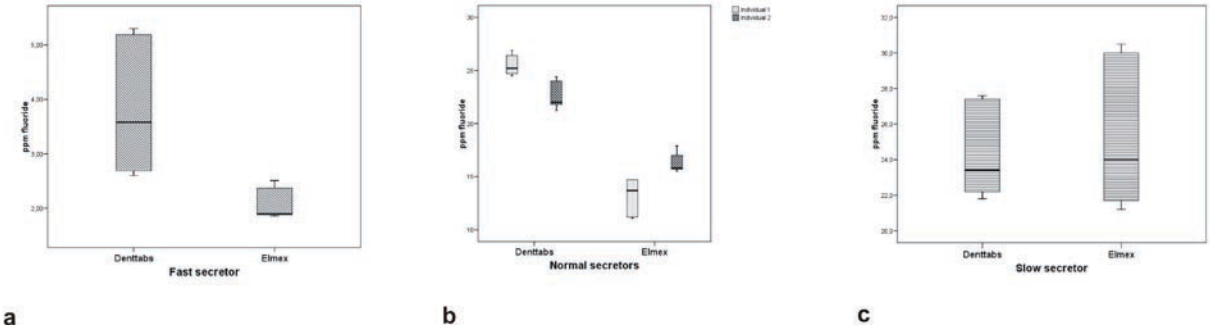
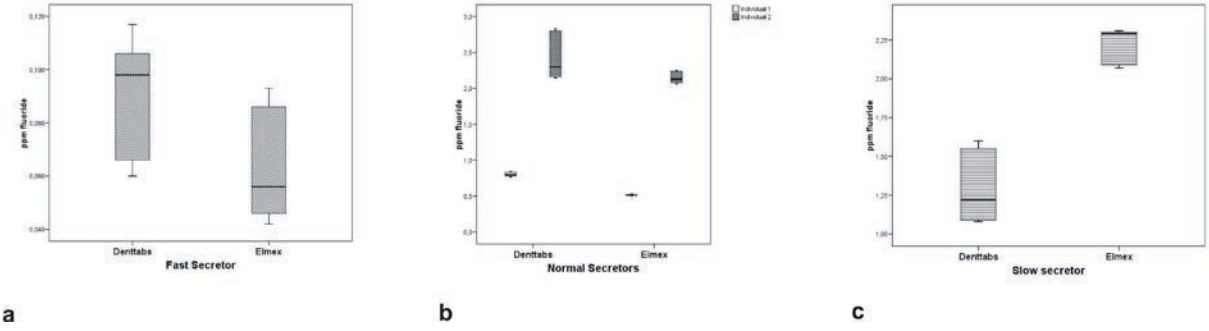


Figure 3. Fluoride content in unstimulated whole saliva from 4 test persons (1 fast saliva secretor (a), 2 normal secretors (b), and 1 slow secretor (c)) 25 minutes after brushing (T3) with DENTTABS® and ELMEX®.



3. Results

The mean fluoride content in saliva at baseline and at the designated time points after tooth brushing is presented in Table 1 and, according to the individual secretion rate, in Figures 1-4 for the fast secretor, the normal secretors and the slow secretor, respectively. The mean baseline value for all 4 subjects was 0.19 ± 0.07 ppm. Immediately after tooth brushing and until T3, a statistically significant increase in the fluoride content was measured in normal and slow secretors, whereas the fast secretor's values were back to baseline already after 25 minutes (T3). The fluoride content remained statistically more elevated ($p<0.05$) in the DENTTABS® cycles immediately after brushing and after 10 minutes compared to ELMEX® cycles. In contrast, the fast secretor did not exhibit significant differences for both products.

Fluoride bioavailability in saliva ranged from 0.06 to 0.23 ppm (baseline), 64.2 to 287.3 ppm (T1), 1.9 to 30.3 ppm (T2), 0.06 to 2.8 ppm (T3) and 0.02 to 0.15 ppm (T4).

There was a significant correlation between the salivary flow rate and the F^- content at T1 and T3 for both DENTTABS® and ELMEX® and also at T2 for ELMEX® (Table 2). The fluoride content varied inversely with the salivary secretion rate (Table 3).

Figure 4. Fluoride content in unstimulated whole saliva from 4 test persons (1 fast saliva secretors (a), 2 normal secretors (b), and 1 slow secretor (c)) 85 minutes after brushing (T4) with DENTTABS® and ELMEX®.

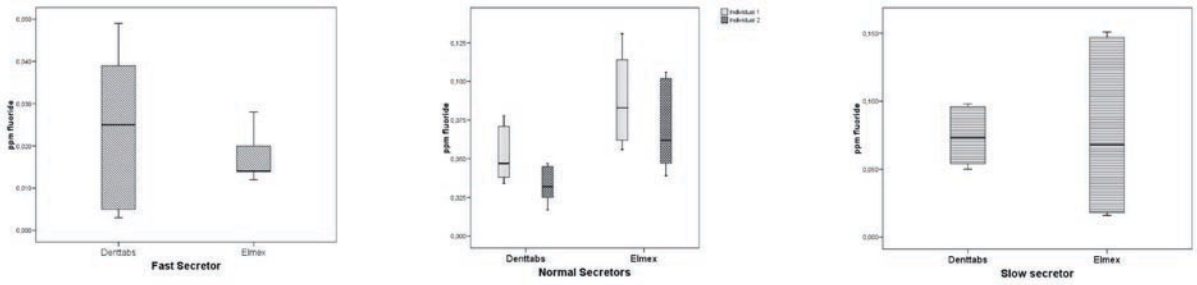


Table 2. Correlation between salivary flow rate (g/min) and fluoride content in saliva (ppm).

Correlation between flow rate and fluoride content					
	Denttabs			*Elmex*	
	R	*p*		*R*	*p*
T1	*0.8*	*0.002*	*T1*	*0.654*	*0.001*
T2	*0.502*	*0.096*	*T2*	*0.691*	*0.013*
T3	*0.728*	*0.007*	*T3*	*0.916*	*0.001*
T4	*0.455*	*0.137*	*T4*	*0.023*	*0.943*

Fluoride retention in whole saliva after using DENTTABS® and ELMEX® is shown in Figures 1-4. Immediately and 10 minutes after tooth brushing, a statistically significant increase was seen both for the DENTTABS® and ELMEX® cycles ($p<0.05$), and the increase was highest for DENTTABS®.

The decrease in fluoride retention after 25 minutes (T3 and T4) did not significantly differ between both groups (Figure 3 and 4).

4. Discussion

It is generally recognised that fluoridated dentifrices are an effective lifelong carrier of fluoride into the oral cavity. The kinetics of fluoride in the oral fluids are well established; the normal concentration in saliva is about 0.02 ppm F^-, which can be elevated by local application of fluoride formulation to some hundred ppm F^- and return to salivary baseline levels in just over 30 minutes [1,10]. It was therefore of experimental and clinical interest whether or not a novel fluoride-containing oral hygiene tablet DENTTABS® can contribute to elevated bioavailability of fluoride in saliva, compared to the conventional dentifrice ELMEX®. Both products contain the same amount of fluoride per application: 4350 ppm F^- per 0.33 g tablet DENTTABS® and 1400 ppm F^- per 1.0 g toothpaste ELMEX®. The aim of the DENTTABS® formulation was the direct solubility of sodium fluoride in saliva, pH adjustment at 5.5 for promoting remineralisation, and optimisation of the polishing effect by microcrystalline hydroxyethylcellulose with less abrasiveness.

Salivary F^- kinetics depend on different factors such as: individual characteristics of saliva, flow rates, age, stimulation effects [12]; properties of F-containing products [13]; volume and application time of these products; and vehicle of fluoride [9]. The interactions between these factors affect the process of F^- clearance from the oral cavity.

Because of the expected high inter-individual variability of saliva secretion and of salivary F^- clearance, four well-calibrated subjects with different secretion rates were selected for the cross-over study. The flow rate was classified into normal, fast and slow

Table 3. Minimal and maximal salivary flow rate (g/min) and corresponding fluoride content in saliva samples (ppm).

Retention time	Test substance	Min flow rate (g/min)	Fluoride content (ppm)	Max flow rate (g/min)	Fluoride content (ppm)
T1 0 min	DENTTABS® ELMEX®	1.40	267.00	3.63	73.00
		1.10	202.00	3.80	70.00
T2 10 min	DENTTABS® ELMEX®	0.32	27.50	1.13	2.70
		0.41	30.30	0.96	15.70
T3 25 min	DENTTABS® ELMEX®	0.21	1.20	1.20	0.06
		0.33	2.10	0.92	0.50
T4 85 min	DENTTABS® ELMEX®	0.17	0.10	1.05	0.04
		0.16	1.60	1.08	0.08

secretors [14,15]. Two subjects had normal flow rates (0.65 ± 0.21 g/min.); one subject was a slow secretor (0.34 ± 0.10 g/min.), and one was a fast secretor (0.91 ± 0.18 g/min.).

Saliva is intrinsically inhomogeneous, contains different phases, i.e. liquid, gaseous and gel phases, and additionally contains cellular debris and microorganisms. Pre-treatment and storage conditions of the saliva samples influence different saliva parameters: electrolytes, buffer, pH, proteins, and viscosity [12]. To avoid obstacles the samples were centrifuged (6000 rpm) for 10 minutes and analysed on the day of collection. Centrifugation leads to a maximal decrease of 15% of the fluoride levels, probably due to precipitation of fluoride with calcium and phosphate [12]. Taking into account this systematic underestimation of fluoride concentrations, the assessment of ions by the fluoride-sensitive electrode represents the true bioavailability at the time of saliva sampling. As expected, the secretion rate of whole unstimulated saliva during and after standardized tooth brushing was inter-individually different. However, the range was the same for both oral hygiene products. The administration of sodium fluoride to be solved directly in saliva, compared to dentifrice as a foam/saliva mixture, seemed to contribute to higher F^- concentrations. In the case of the fast secretor this effect is obviously masked by the rapid flow rate and extensive deglutition. These results underline that assessment of kinetics of fluoride in saliva should be based on individual multiple subject-related measurements instead of pooled group results.

Immediately after brushing the fluoride concentration of the slurry/saliva mixture was elevated to 100-280 ppm for normal secretors as well as for the slow secretor, and the F^- level of the DENTTABS® cycles was significantly higher compared to ELMEX®. In contrast, the fast secretor exhibited F^- bioavailability levels of only 61-74 ppm, and there was no difference between the two fluoride sources.

The normal secretors demonstrated the same kinetics of elevated fluoride concentrations in favour of DENTTABS® for the next 25 minutes, and levels fell back down to the baseline after 85 minutes after brushing. The fast secretor's levels were already back to baseline after 25 minutes because of the high clearance, minimizing the F^- bioavailability by rapid deglutition. Like the normal secretors, the slow secretor exhibited elevated F^- levels for more than 25 minutes, but there was not different levels for the tablet cycles.

The F^- bioavailability immediately after tooth brushing as well as the clearance within 10 to 85 minutes is strongly related to the individual saliva flow rate. This is demonstrated by the differences in fluoride concentrations amongst normal secretors, slow secretor, and fast secretor. In contrast to other experiments where results of groups of 10 to 30 subjects are pooled [8,16], the novel finding of this study demonstrates that fluoride kinetics, like kinetics of most drugs, is strictly influenced by individual factors of the subjects. It seems, therefore, that the salivary flow rate plays a major role in the F^- availability after local administration of oral hygiene products. In 1990 Dawes and Weatherell [1] already stressed the fact that fluoride clearance is related to the salivary flow rate and is also not constant throughout the mouth, but shows considerable site-specificity.

Recently it has been demonstrated that elevated fluoride products enhance remineralization of advanced enamel lesions, at least under well controlled in-vitro conditions [17]. Therefore, the higher F^- concentration in saliva after administration of oral hygiene tablets compared to dentifrice may contribute to optimized remineralization conditions at the tooth surfaces at risk.

Fluoride bioavailability in saliva is dependent upon the applied fluoride concentration [18,19] and the mouth rinsing procedure [20,21]. A previous study showed that the use of Olafluor® results in a higher salivary fluoride level than the use of NaF [22]. However, a number of studies investigated the fluoride concentration in saliva after the application of different formulations and found only minor differences between amine fluoride, NaF and sodium monofluorphosphate [4,21]. In this study the fluoride-containing oral hygiene tablets clearly demonstrated an elevated bioavailability for around 30-60 minutes after brushing in the slow and normal secretors.

5. Conclusions

In conclusion, increased fluoride concentrations in saliva following standardized tooth brushing were documented for both a novel sodium fluoride-containing oral hygiene tablet and a well proven traditional amine fluoride-containing dentifrice. The bioavailability of fluoride from tablets, solved in saliva, was significantly higher compared to the dentifrice. Finally, the kinetics of fluoride in saliva differ rather strongly on an individual basis and depend upon the oral hygiene product formulation.

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