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EFFECT OF TOPICALLY APPLIED AGENTS ON ENAMEL

IV. EXPERIMENTS *IN VITRO* WITH IRON FLUORIDE SOLUTIONS

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Laboratory experiments supported by theoretical considerations indicated that ferric fluoride complexes can increase the acid resistance of the enamel surface (1, 2). With this in mind the authors decided that the caries prophylactic value of topical application of iron fluorides deserves a close examination.

In preliminary experiments (3) newly prepared solutions which were 0.1-molar as to ferrous chloride, 0.1-molar as to ferric chloride, and 0.2-molar as to sodium fluoride were found to have only a very slight protective effect on the enamel. After a storage time of 1—12 days, however, the same solutions markedly increased the resistance of the enamel. For clinical use solutions to be applied topically must be well defined. Therefore, it was decided that the chemical reactions underlying the results obtained in the preliminary experiments should be examined. This is the purpose of the present investigation.

The behaviour of iron fluorides as deduced from the literature

The following compilation is based on information in representative reports of the chemistry of iron fluorides (4—15).

With fluoride ions ferric ions form all possible complexes between $[FeF]^{2+}$ and $[FeF_6]^{3-}$. The concentration of the different complexes in a solution is determined by the relation between the amount of ferric ions and the amount of fluoride ions present. In solutions with a low relation between fluoride ions and ferric ions (e.g. 1: 1 or 2: 1) the mono- and difluoro-complexes are dominating. At a high relation (e.g. 6: 1 or 5: 1) the solutions contain complexes in which almost all of the six coordination positions of the ferric ions are occupied by fluoride ions. In solutions with a relation between fluoride ions and ferric ions higher than 6: 1 practically only the hexafluoro complexes are present. Since the values of the formation constants of the various ferric fluoride complexes are large the complexes are formed at low concentrations of fluoride ions and ferric ions. The formation constants indicate that fluoride ions are more easily released from the higher complexes than from the lower complexes.

In "ferric fluoride" solutions with a relation between ferric ions and fluoride ions of 1: 1, 1: 2, or 1: 3 precipitates are formed at pH-levels about 3.5 owing to hydrolysis. At higher relations precipitates are formed only at higher pH-levels. These precipitates can be $Fe(OH)_3$, $Fe(OH)_2F$, and FeF_3. In the presence of various metal ions complex salts as for instance fluoroferriates of the types $MFeF_4$, M_2FeF_5, and M_3FeF_6 can be precipitated (M = univalent metal ion). Fluoroferriates with sodium and potassium are reported to be more easily precipitated than those with ammonium.

The ferric ions form strong complexes with hydroxyl ions and phosphate ions. This capacity is greatly diminished in the presence of fluoride ions.

The fluoride complex forming tendency of the ferrous ion is much weaker than that of the ferric ion. In the reaction $Fe^{2+} + F^- = [FeF]^+$ the formation constant for $[FeF]^+$ is smaller than 30. Hence in fluoride solutions containing ferrous and ferric ions the fluoride ions are preferentially bound to the ferric ions. As ferrous ions are rapidly oxidized, ferrous fluoride solutions very soon will yield ferric fluoride complexes. Ferrous fluoride is sparely soluble and double salts of unknown structures, $MFeF_3$ and M_2FeF_4, can be precipitated.

Theoretical conditions for an iron fluoride solution for topical application

The working hypothesis underlying the present experiments with iron fluoride solutions is that a combined effect of iron ions and fluoride ions will give a higher degree of protection against dental caries than is obtainable with alkali fluoride solutions. Consequently, it was the intention to precipitate iron ions together with fluoride ions in the superficial layers of the enamel. Topical applications of sodium fluoride solutions bring about an initial precipitation of calcium fluoride. Thus, if iron ions as well as fluoride ions are to be incorporated in the enamel surface layers it is necessary to compose the iron fluoride solution in such a way that calcium fluoride is not precipitated initially during the application. This condition can be fulfilled only if the solution contains ferric ions, as ferric ions form strong complexes with fluoride ions, while ferrous ions only form weak complexes.

It seems probable that the relation between fluoride ions and ferric ions are to be kept low (for instance 1: 1, 2: 1, or 3: 1), as fluoride ions are released more easily from the higher ferric fluoride complexes and thus possibly facilitating the precipitation of calcium fluoride. This can be illustrated as follows,

$$2\left[FeF_6\right]^{3-} + Ca^{2+} = 2\left[FeF_5\right]^{2-} + CaF_2.$$

The possibility of precipitating calcium fluoride is great if the relation between fluoride ions and ferric ions is greater than 6: 1. Principally such solutions may act on the enamel as sodium fluoride solutions. This is examplified in the following reaction,

$$n\left[FeF_6\right]^{3-} + mF^- + Ca^{2+} = n\left[FeF_6\right]^{3-} + (m-2)\,F^- + Ca\,F_2.$$

If the relation between fluoride ions and ferric ions is very low, the initial precipitates formed on the enamel surface may consist of ferric hydroxide or ferric hydroxide — ferric phosphate gels. Such precipitates must be avoided, as they may increase the vulnerability of the enamel to dental caries (13). With this in view it seemed necessary to examine the precipitating effect of the addition of calcium phosphate to "ferric fluoride" solutions.

Titration of acid calcium phosphate solutions containing varying amounts of ferric and fluoride ions

Material and method

A 0.02-molar stock solution of $CaHPO_4$, pH 0.67 was prepared by dissolving $CaHPO_4$ in hydrochloric acid. In this solution ferric chloride and sodium fluoride were dissolved. 10 ml of each of the solutions thus prepared were then titrated with 0.1-molar NaOH up to pH-values at which precipitates were formed and remained visible after thorough stirring. These values and the amounts of NaOH added to the solutions were registered.

The molarity of ferric chloride and sodium fluoride in the titrated solutions are given in Table 1.

Table 1

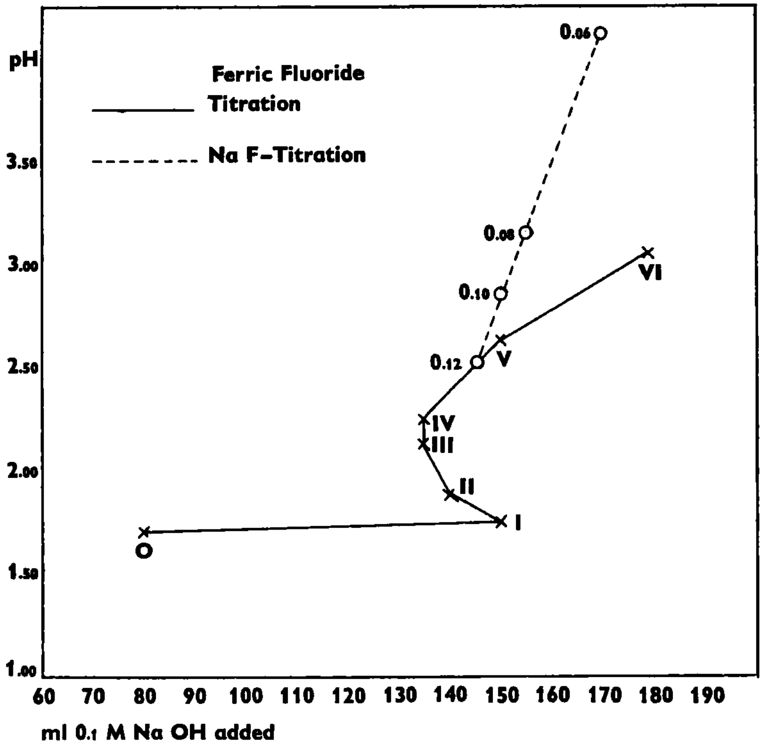
Solution	mols $FeCl_3$	mols NaF
0	0.05	—
I	0.05	0.05
II	0.05	0.10
III	0.05	0.15
IV	0.05	0.20
V	0.05	0.25
VI	0.05	0.30
0.06	—	0.06
0.08	—	0.08
0.10	—	0.10
0.12	—	0.12

Results

The registrations are presented in the diagram on page 271. They indicate that the precipitates formed in solutions with the ratio Fe : F = 1 : 2, 1 : 3, or 1 : 4 contain iron and fluorine. Therefore, solutions of this kind ought to be instrumental in forcing iron ions as well as fluoride ions into the superficial layers of the enamel.

TOPICAL APPLICATIONS IN VITRO

The applications were performed and the results evaluated according to the modified method of *Mörch, Torell* and *Hals* (3).



Application series 1

The solution employed was 0.1-molar as to ferric chloride and 0.2-molar as to sodium fluoride. The pH-value of the solution was adjusted to 2.3.

The results are given in Table 2.

Table 2. 0.1 M $FeCl_3$ + 0.2M NaF, pH 2.3 Freshly prepared solutions

Number of exper.	Results			
	Positive difference			No difference
	Marked	Slight	V. slight	
15	0	3	6	6

Discussion: The results were only slightly better than the results obtained by the present authors with sodium fluoride solutions (See Table 4). Contrary to the first experiments (3) no case of marked positive difference was observed. Therefore, it was deemed possible to obtain more effective solutions. From a theoretical point of view this could probably be done by addition of calcium phosphate to the present solutions with simultaneous lowering of the pH-value. This ought to prevent the formation of basic ferric phosphate without destroying the enamel.

Application series 2

The solution employed was prepared in the following way: 0.02-molar $CaHPO_4$-solutions (pH = 0.32) were made 0.1-molar as to ferric chloride and 0.2-molar as to sodium fluoride. To the solutions were then added drops of strong sodium hydroxide solution up to the point where a slight opalescence remained visible after thorough stirring. At this moment the pH was within the range 1.55—1.85. The solutions were stored in poly-ethylen-bottles, treated according to the principles of *Hals, Mörch* and *Torell* (16).

The results are given in Table 3.

Table 3. 0.1 M $FeCl_3$ + 0.2 M NaF + 0.02 M $CaHPO_4$ (pH 0.32)

Number of exper.	Present pH	Storage time	Results			
			Positive difference			No difference
			Marked	Slight	V. slight	
10	1.55	0	—	3	4	3
4	1.70	0	—	1	2	1
3	1.82	1 day	1	1	1	—
3	1.58	4 days	—	3	—	—
3	1.62	6 days	—	1	2	—
2	1.72	6 days	—	1	1	—
3	1.55	8 days	1	2	—	—
1	1.55	17 days	1	—	—	—
1	1.56	29 days	—	1	—	—
30	—	—	3	13	10	4

Discussion: The results obtained with this stable and well defined solution are decidedly better than the results obtained in application series 1. They are also better than the results obtained by the present authors with sodium fluoride solutions and reproduced in Table 4.

Table 4. 0.5 M NaF, pH 6.63

Number of experiments	Results				
	Positive difference			No difference	Negative difference
	Marked	Slight	V. slight		
110	0	7	5	96	2

In the preliminary experiments with ferric fluoride solutions ferrous ions were also employed. With the results of *Torell* (1) in mind it might be argued that the significance of the ferrous ions ought to be studied.

Application series 3

The solution employed was prepared in the following way: 0.02-molar $CaHPO_4$-solutions ($pH = 0.32$) were made 0.1-molar as to ferric chloride, 0.1-molar as to ferrous chloride, and 0.2-molar as to sodium fluoride. To the solution were then added drops of a strong sodium hydroxide solution up to the point where a very slight opalescence remained visible after thorough stirring. The solutions were stored in polyethylen-bottles as in application series 2.

The results are given in Table 5.

Table 5. 0.1 M $FeCl_3$ + 0.1 M $FeCl_2$ + 0.2M NaF + $CaHPO_4$ (0.02 M)

Number of exper.	Present pH	Storage time	Results			
			Positive difference			No difference
			Marked	Slight	V. slight	
3	1.40	1 day	2	—	1	—
3	1.25	4 days	1	1	—	1
3	1.27	6 days	1	1	1	—
3	1.20	8 days	1	2	—	—
1	1.15	17 days	1	—	—	—
1	1.15	29 days	—	—	1	—
14	—	—	6	4	3	1

Discussion: The results suggest that the effect of ferric fluoride solutions may be improved by the presence of ferrous ions.

Comments to application series 1, 2, and 3

The results of series 1, 2, and 3 show that certain iron fluoride solutions may increase the acid resistance of dental enamel to a higher degree than sodium fluoride solutions. This conclusion is strengthened by the results of a number of pilot experiments, in which the solutions employed were varied as to pH-value and composition. The results of these pilot experiments are given in Table 6.

Table. 6. *Iron fluoride solutions of varying composition and pH-values*

Number of exper.	Results				
	Positive difference			No difference	Negative difference
	Marked	Slight	V. slight		
53	5	15	16	16	1

SUMMARY

The experiments *in vitro* reported in the present paper were performed in order to study the possibility of using iron fluoride solutions in caries prophylaxis. The composition of the solutions examined were determined on the basis of a review of the chemistry of iron fluorides supplemented with an experimental study.

The results of the experiments indicate that applied topically certain iron fluoride solutions will increase the acid resistance of dental enamel. As the increase was found to be greater than that obtained by applications of sodium fluoride solutions it seems possible that iron ions in combination with fluoride ions may be instrumental in reducing dental caries.

RESUME

EFFET SUR L'EMAIL D'AGENTS APPLIQUES LOCALEMENT
IV. EXPERIENCES IN VITRO AVEC DES SOLUTIONS DE FLUORURE DE FER

Les expériences *in vitro* dont rend compte le présent article ont été faites dans le but d'étudier la possibilité d'utiliser des solutions de fluorure de fer dans la prévention de la carie. La composition des solutions étudiées a été établie en se basant sur un examen de la chimie des fluorures de fer complété par une étude expérimentale.

Les résultats des expériences indiquent que, lorsqu'elles sont appliquées localement, certaines solutions de fluorure de fer provoquent une augmentation de la résistance de l'émail dentaire aux acides. L'augmentation mise en évidence étant plus grande que celle que l'on obtient au moyen d'applications de solutions de fluorure de sodium, il semble possible que les ions fer en combinaison avec les ions fluorure soient efficaces comme moyen de réduction de la carie dentaire.

ZUSAMMENFASSUNG

DIE WIRKUNG VON LOKAL APPLIZIERTEN LÖSUNGEN AUF DEN SCHMELZ

IV. Untersuchungen in vitro mit Eisenfluoridlösungen

Die Untersuchungen der vorliegenden Arbeit wurden durchgeführt um die Möglichkeit der Anwendung von Eisenfluoridlösungen in der Kariesprophylaxe zu beleuchten. Die Zusammensetzung der zur Anwendung gebrachten Lösungen wurde mittels Erwägungen über die Chemie der Eisenfluoridlösungen sowie eigener Versuchen festgelegt.

Die Ergebnisse der Untersuchungen lassen vermuten, dass lokale Applikation von gewissen Eisenfluoridlösungen die Säureresistenz des Zahnschmelzes erhöhen kann. Da diese Erhöhung grösser war als die durch Natriumfluoridlösungen hervorgerufene, scheint es möglich, dass Eisenionen, mit Fluoridionen kombiniert, ein kariesreduzierendes Mittel sein könnten.

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