

# TITANIUM TETRAFLUORIDE AND DENTAL CARIES: A SYSTEMATIC REVIEW

## TETRAFLUORETO DE TITÂNIO E CÁRIE DENTÁRIA: UMA REVISÃO SISTEMÁTICA

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### ABSTRACT

The aim of this systematic review was to evaluate the effectiveness of titanium tetrafluoride as a preventive or cariostatic agent against caries. The databases used to find the articles analyzed were MEDLINE LILACS, and BBO. In MEDLINE and LILACS the search strategy utilized was “titanium” [Words] and “tetrafluoride” [Words] and Spanish or English or Portuguese [Language], whereas In BBO “titânio” [Words] and “tetrafluoreto” [Words] and Espanhol or Inglês or Português [Language]. Out of a total of 42 studies found, which assessed possible preventive/cariostatic effects of titanium tetrafluoride against caries *in vivo*, only 2 were selected. In both studies, titanium tetrafluoride was shown to be effective against caries. However, given that the quality and consequently the validity of these two clinical studies are questionable, their results do not allow to conclude that titanium tetrafluoride is effective against caries clinically.

**Uniterms:** Dental caries; Titanium; Tetrafluoride; Cariostatic agents.

### RESUMO

Esta revisão sistemática foi desenvolvida com o objetivo de avaliar a eficácia do tetrafluoreto de titânio como agente preventivo contra a cárie e/ou cariostático. Foram revisados, através da BIREME, artigos publicados nas revistas indexadas nas bases de dados MEDLINE, LILACS e BBO, utilizando as estratégias de busca titanium [Palavras] and tetrafluoride [Palavras] and Spanish or English or Portuguese [Idioma] na MEDLINE e no LILACS, já na BBO foram utilizados titânio [Palavras] and tetrafluoreto [Palavras] and Espanhol or Inglês or Português [Idioma]. De um total de 42 trabalhos diferentes encontrados, que avaliaram os efeitos preventivo/cariostático do tetrafluoreto de titânio contra a cárie *in vivo*, apenas 2 foram selecionados. Em ambos os estudos, o tetrafluoreto de titânio se mostrou efetivo contra a cárie. No entanto, considerando que a qualidade e, conseqüentemente, as validades desses poucos trabalhos clínicos existentes estão abertas para alguns questionamentos, conclui-se que os resultados apresentados não nos permitem dizer se o tetrafluoreto de titânio apresenta benefícios nos cuidados relacionados à cárie.

**Unitermos:** Cárie dentária; Titânio; Tetrafluoreto; Cariostáticos.

### INTRODUCTION

Fluorides are the most frequently used agents applied to the dental enamel surface to try to obtain greater resistance against caries. However, their effectiveness on patients with high caries activity has been put into question<sup>8</sup>. Due to a number of animal and *in situ* studies showing that titanium fluoride (TiF<sub>4</sub>) provides a higher level of protection than other fluorides against caries, TiF<sub>4</sub> has recently attracted considerable interest. The first *in vitro* tests performed in

1972 gave rise to studies on the effect of titanium tetrafluoride on dental enamel as a protective agent against caries<sup>5,10</sup>. Since then, several studies involving titanium tetrafluoride have been undertaken in an attempt to confirm its cariostatic properties. The findings of these studies reveal that when titanium tetrafluoride is applied to the dental enamel surface there is formation of fluoridated apatite, decreasing enamel solubility due to both an increase in the content of fluoride and formation of a film which protects the enamel against the action of acids<sup>2,5,10</sup>.

A number of studies report that in addition to its cariostatic effects, titanium tetrafluoride may also be used for other purposes such as in the treatment of dentinal hypersensitivity<sup>6</sup>, for the prevention of microleakage and secondary caries in cavities prepared in dentin or for decreasing root permeability by modifying the smear layer<sup>1,9,12</sup>.

Despite this, the entire effect and all the beneficial properties that this drug may or may not possess are still not completely understood. Studies are underway to try to further investigate its promising properties, effectiveness, duration of use, as well as its optimal concentration. In an attempt to provide greater insight into such issues, this systematic review was carried out to evaluate the effectiveness of titanium tetrafluoride against caries.

## METHODOLOGY

### Search strategy

Internet research: articles from journals indexed in MEDLINE, LILACS (Latin American and Caribbean Literature on the Health Science) and BBO (Brazilian Bibliography of Dentistry) databases were accessed via BIREME (Latin American and Caribbean Center on Health Sciences Information – www.bireme.br). The search strategy used in MEDLINE and LILACS was “titanium” [Words] and “tetrafluoride” [Words] and Spanish or English or Portuguese [Language], whilst in BBO “titânio” [Words] and “tetrafluoreto” [Words] and Espanhol or inglês or Português [Language].

The only studies selected were human clinical trials which assessed possible preventive/cariostatic effects of titanium tetrafluoride against caries. *In vitro* studies, *in situ* studies, clinical trials on animals and studies which assessed other properties of titanium tetrafluoride were excluded.

## RESULTS

Seventeen of the studies found in MEDLINE were carried out between 1993 and 2005 and 17 between 1966 and 1992, whereas in LILACS 3 studies were found and 9 in BBO. The 3 studies found in LILACS may also be found in BBO, where one article being referenced twice (once as a dissertation and once as a journal publication). From a total of 42 different studies found (34 in English and 8 in Portuguese), only 2 *In vivo* studies assessed the preventive/cariostatic effects of titanium tetrafluoride against caries, among which 1 was encountered in MEDLINE, between the years of 1966 and 1992 and 1 between 1993 and 2005. Figure 1 summarizes the studies analyzed indicating their objectives, methodologies and results.

## DISCUSSION

Randomized controlled clinical trials are studies that carry more weight when evaluating the effectiveness of clinical interventions, since they are extremely rigorous and are aimed at measuring and comparing the outcomes of two or more interventions.

The two studies selected for the present review<sup>2,11</sup> suggest that TiF<sub>4</sub> is effective against caries. However, the quality and consequently the validity of these studies are questionable.

An analysis of the quality of these studies reveals that they are both controlled studies, although only one of them is blind where it was reported that the individuals involved did not know which treatment was being performed or assessed in order to avoid the influence of confounding factors.

With regard to sample size and method of selection, these were not considered ideal. In Bbüyükyilmaz et al (1994)<sup>2</sup> the number of teeth involved were insufficient for any conclusions to be drawn whereas in Reed and Bibby (1976)<sup>11</sup> it is not clear whether the sample was randomly selected.

Both studies<sup>2,11</sup> used 1% TiF<sub>4</sub> for 1 minute. These results differ from those of current trials focusing on the frequency of fluoride use, where it has been observed that fluorides are more effective when applied with greater frequency and in lower concentrations<sup>8</sup>.

When compared to other fluorides, TiF<sub>4</sub> presented an increase in caries that was 33% lower than APF<sup>11</sup>. In other studies performed on animals, comparing TiF<sub>4</sub> to SnF<sub>2</sub>, APF and CuF<sub>2</sub>, the experimental group treated with TiF<sub>4</sub> was the only that did not present root caries<sup>7</sup>. No significant differences were encountered in caries reduction on buccal + lingual surfaces, occlusal fissures and in total caries when TiF<sub>4</sub> was compared to NaF with pH 1.5 or 7<sup>13</sup>.

Perhaps the supremacy of TiF<sub>4</sub> in relation to other fluorides, found in some studies, are due to the mechanism of action of TiF<sub>4</sub> which, in addition to the formation of fluoridated apatite, which reduces enamel solubility, also produces a titanium dioxide layer forming a protective film against acids<sup>2,5,7</sup>.

With respect to this protective film, promising results were observed, since despite the masticatory and abrasive forces of brushing and of food particles this protective layer, resultant from TiF<sub>4</sub> application, was still present up to 1 year later<sup>3</sup>.

As to the protection against cariogenic attacks, it was observed that TiF<sub>4</sub> prevented root caries formation<sup>7</sup>, but when faced with a more intense attack, it may have only modified the pattern of carious lesion formation<sup>10</sup>.

A number of studies evaluated reduction of lesion depth and mineral loss after TiF<sub>4</sub> application and obtained different results. While a 56% reduction in lesion depth was found in one study<sup>4</sup>, another presented 37%<sup>2</sup>. In relation to mineral loss, the values were 62%<sup>4</sup> and 14%<sup>2</sup>, respectively. However, the distinct conditions under which such studies were performed must be considered, since one involved a clinical trial with a very small sample size that used TiF<sub>4</sub> at 1%<sup>2</sup>,

whereas the other was an *in situ* study using a concentration of 4% and similarly a small sized sample<sup>4</sup>.

These studies on animals<sup>7,13</sup> and *in situ*<sup>4,5,10</sup> also show satisfactory results of TiF<sub>4</sub> against dental caries. However randomized controlled clinical trials are necessary to confirm the effectiveness of TiF<sub>4</sub> clinically.

## CONCLUSIONS

Based on the articles evaluated, and considering both the paucity of human clinical trials and the quality of the studies analyzed, the results presented do not allow to conclusively state that titanium tetrafluoride application is beneficial against caries in the clinic. More clinical studies are warranted to address the many omissions identified in the studies reviewed. Hopefully, such clinical trials will provide in the near future a clearer picture regarding the effectiveness of titanium tetrafluoride against dental caries.

## REFERENCES

- 1- BRZOZOWSKI ME. Influência da aplicação do tetrafluoreto de titânio na permeabilidade dentinária do sistema endodôntico. São Paulo; 2002. [Tese de doutorado - Faculdade de Odontologia da USP].
- 2- Büyükyılmaz T, Tangugsorn V, Ogaard B, Arends J, Ruben J, Rolla G. The effect of titanium tetrafluoride (TiF<sub>4</sub>) application around orthodontic brackets. Am J Orthod Dentofacial Orthop. 1994 Mar;105(3):293-6.
- 3- Büyükyılmaz T, Sen BH, Ogaard B. Retention of titanium tetrafluoride (TiF<sub>4</sub>), used as fissure sealant on human deciduous molars. Acta Odontol Scand. 1997 Apr;55(2):73-8.
- 4- Büyükyılmaz T, Ogaard B, Duschner H, Ruben J, Arends J. The caries-preventive effect of titanium tetrafluoride on root surfaces *in situ* as evaluated by microradiography and confocal laser scanning microscopy. Adv Dent Res 1997 Nov;11(4):448-52.
- 5- Castro RAL. Efeito da aplicação de tetrafluoreto de titânio sobre o esmalte dentário humano oclusal: um estudo *in situ*. Rio de Janeiro; 2001. [Dissertação de Mestrado - Faculdade de Odontologia da UFRJ].

TITLES	OBJECTIVES	METHODOLOGIES	RESULTS
The effect of titanium tetrafluoride (TiF <sub>4</sub> ) application around orthodontic brackets (BÜYÜKYILMAZ et al, 1994) <sup>2</sup>	Investigate the cariostatic potential of a 1% TiF <sub>4</sub> solution applied topically around orthodontic brackets and examine the characteristics of the superficial layer.	Randomized controlled clinical trial. Sample: 20 premolars of 7 adolescents. 40% Phosphoric acid was applied for 1 min to all teeth, and orthodontic brackets were subsequently bonded. The teeth were then separated, 10 serving as controls and 10 treated with 1% TiF <sub>4</sub> around the brackets for 1 min. After 4 weeks, all the teeth were extracted and assessed in regard to reduction in lesion depth and mineral loss by microradiography and scanning electronic microscopy (SEM).	Microradiography: There was a significant difference between the test and control groups. A 37% reduction in lesion depth and 14% reduction in mineral loss in the test group. SEM: presence of a superficial layer.
Preliminary report on the effect of topical applications of titanium tetrafluoride on dental caries (REED e BIBBY, 1976) <sup>11</sup>	Assess the effect of topical applications of 1% titanium tetrafluoride on dental caries	Blind controlled clinical trial. Sample: 204 children aged 11-13 (144 test group and 60 control). The test group children received an annual topical application of TiF <sub>4</sub> at 1% (1 min) on one side of the mouth and APF (4 min) on the other side. This procedure was repeated during 2 consecutive years and clinically assessed at 3 different time points.	TiF <sub>4</sub> /APF: 1 <sup>st</sup> year – p< 0.004 2 <sup>nd</sup> year – not significant 3 <sup>rd</sup> year – p< 0.04 TiF <sub>4</sub> /control: 1 <sup>st</sup> year – p< 0.004 2 <sup>nd</sup> year – p< 0.004 3 <sup>rd</sup> year – p< 0.004 TiF <sub>4</sub> presented 33% less caries increment than APF and 50% less than control.

FIGURE 1- Studies analyzed and their objectives, methodologies and results. Natal, RN, Brazil, 2005

- 6- Charvat J, Söremark R, Li J, Vacek J. Titanium tetrafluoride for treatment of hypersensitive dentine. *Swed Dent J.* 1995;19(1-2):41-6.
- 7- Cordeiro JGO. The effect of various fluoride compounds on the development of experimental root surface caries in hamsters. *Bull Tokyo Med Dent Univ.* 1995 Dec;42(3):105-16.
- 8- Hausen H. How to improve the effectiveness of caries-preventive programs based on fluoride. *Caries Res.* 2004;38:263-7.
- 9- Kazemi RB, Sen BH, SpanberG LS. Permeability changes of dentine treated with titanium tetrafluoride. *J Dent.* 1999 Sep;27(7):531-8.
- 10- Morais AP, Souza IPR, Chevitaress O. Estudo in situ do esmalte dental humano após aplicação de tetrafluoreto de titânio. *Pesqui Odontol Bras.* 2000 Abr./Jun;14(2): 137-43.
- 11- Reed AJ, Bibby BG. Preliminary report on effect of topical applications of titanium tetrafluoride on dental caries. *J Dent Res.* 1976 May/Jun;55(3):357-8.
- 12- Sen BH, Büyükyilmaz T. The effect of 4% titanium tetrafluoride solution on root canal walls - a preliminary investigation. *J Endod.* 1998 Apr;24(4):239-43.
- 13- Skartveit L, Spak CJ, Tveit AB, Selvig KA. Caries-inhibitory effect of titanium tetrafluoride in rats. *Acta Odontol Scand.* 1991;49:85-8.