Historical and bibliometric notes on the use of fluoride in caries prevention

P. Zampetti*, A. Scribante**

Section of Dentistry, Department of Clinical, Surgical, Diagnostic and Paediatric Sciences, University of Pavia, Pavia, Italy
**Professor of History of Dentistry*
*** Professor of Oral Pathology*

e-mail: andrea.scribante@unipv.it

DOI 10.23804/ejpd.2020.21.02.10

Abstract

Aim The aim of the present report was to highlight historical and bibliometric aspects of fluoride in dentistry.

Methods Study design: In the first part of the manuscript, history of fluoride has been reported. In the second part, some bibliometric considerations have been explained. The historical research evaluated the first documents about fluoride in dentistry. The bibliometric research considered Scopus-indexed documents from 1945 to 2019.

Results Historical search showed the consistent presence of documents since 1803, even if modern research started in the 1930s. Statistics: Descriptive statistics of documents about fluoride showed a constantly increasing interest on the topic, starting from 1965 to nowadays.

Conclusions The topic of fluoride has a long history in dental practice, and future interesting research is needed in order to combine this well-known inorganic, monatomic anion with new emerging technologies.

KEYWORDS Fluoride; History; Bibliometric; Analysis; Paediatric dentistry; Restorative dentistry; Orthodontics; Enamel; Tooth.

Introduction

Before fluoride applications, hygiene, prophylaxis and stomatology had not made substantial contributions to the reduction of the aetiological problems related to dental caries; it was only in the 1930s and 1940s that a series of studies and research began that made it possible to understand the unquestionable importance of fluoroprophylaxis [Zampetti and Riva, 2020]. In truth, as early as 1803 Domenico Morichini found fluoride in an elephant's fossil molar tooth; later he succeeded in isolating hydrofluoric acid from human bones and teeth, postulating the probable relationship between the fluoride content of the tooth and its morbid processes.

"As far as I know, a chemist has never suspected, and much less proven, the existence of fluoric acid in animal substances. This consideration makes me believe that it will not be without interest in a series of tests I have instituted to demonstrate that fluoric acid combined with lime exists in the enamel of a fossil elephant tooth found in the vicinity of Rome; and what is most surprising in the enamel of human teeth. This argument, although it may seem at first a pure chemical curiosity, deserves in my opinion some attention for the usefulness that could result from the knowledge of the diseases of the teeth, which are born originally or propagate in the enamel of the same". This work was published posthumously; Morichini's research on fluoride in enamel began around 1802 and continued for about a decade. The author communicated the first results in 1803 to the Italian Society of Mathematical and Physical Sciences [Morichini, 1852].

On the basis of these considerations a German physician, Erhard, in 1875 presented a report to the XIV congress of the Central Association of German Dentists "on the way to nourish the teeth with artificial means", that is with fluoride tablets. The "fluoride tablets" were first manufactured in 1874 in the Glocken Apoteke (Bell Pharmacy) in Emmendingen, Brisgau, Erhard's hometown Five decades later, in 1900, a doctor from Naples, Italy, Stefano Chiaia, observed how some of his fellow citizens showed teeth that had brown spots but were particularly resistant to caries. The scholar pointed out how such a finding could be ascribable to the presence, in the drinking water of some areas of the city, of fluoride. Similar observations were made in 1901 by Eager, who noticed the very particular aspect of the enamel of the teeth of the inhabitants of Pozzuoli (Naples). Eager called the teeth with this particularity "Chiaia teeth", after the name of the scholar who first observed them. In fact a tooth with more fluoride content is less prone to caries disease, needs less conservative and prosthodontic treatments [Askar et al., 2020], also reducing the risk of occlusal trauma [Meynardi et al., 2018].

In 1915 the phenomenon of spotted enamel was described by McKay and Black, who later demonstrated that the frequency of carious disease was much less represented in individuals with spotted teeth than in others. On the basis of these studies, around the 1930s, research was begun in the Soviet Union and the United States of America into the inhibiting action of fluoride on dental caries; in 1937 scholars of the Soviet Union suggested the topical application of a toothpaste composed of sodium fluoride, calcium carbonate and glycerin in equal parts, for the treatment of hypersensitivity of cervical regions of the teeth, while two years later other Russian researchers hypothesised that sodium fluoride applied to dentin constituted a barrier against the action of germs, since chemically binding the fluoride ion to the calcium of dentin itself, it formed a hard and dense layer [Palazzi, 1951].

Once these results were obtained, it was decided to administer fluorine for preventive purposes; one of the

methods used was that of fluoridation of drinking water, which is now widely used. This system was experimented starting from the 1940s in the United States, in Michigan, in the city of Grand Rapids; following the example of this method of use, we gradually moved towards the fluoridation of aqueducts. Similarly, great impetus was given to the prophylaxis with fluoride by those who supported its usefulness with other routes of administration, such as the use of fluorinated tablets or, more widely, topical applications.

In 1942 the American Cheyne, assuming that also dental tissues could react with fluoride ion, like bone tissue, experimented with the topical application of an aqueous solution of 0.05% potassium fluoride on preschool children; the application proposed by the author lasted four minutes and was repeated at intervals of about three months for four months [Cheyne, 1942]. After one year of experimentation he observed that in treated subjects the incidence of caries was less than 50% compared to untreated individuals. Similar conclusions were reached by Bibby, about two years later, using sodium fluoride [Bibby, 1944], as experimented in the same period by Knutson and Armstrong [1945]; the treatment proposed by these authors involved the application of a solution of 2% sodium fluoride, applied to eight consecutive weeks with bi-weekly validity for children aged 6 to 12 years. The results obtained showed a 40% reduction in caries after two years of experimentation. Other authors, later, moved towards the use of stannous fluoride [Muhler and Day, 1950]. Encouraged by the good results obtained with the local application of fluorinated solutions, other scholars proposed the use of fluoride toothpaste. Initially, this method was not positive: Bibby, who already, as we have seen, managed to obtain flattering results in the field of local prophylaxis, thought of replacing the aqueous solution of sodium fluoride with a fluorinated toothpaste; after experimenting on 386 subjects in his garrison, he came to the conclusion that the applications in paste should be considered ineffective. Probably, admits the author, brushing of the teeth was poorly performed by the patients, thus preventing the application of fluoride on every point of the tooth surface, especially in the interproximal spaces [Bibby, 1948]. However, from the 1950s onwards, many researchers and scholars established the effectiveness of this prophylactic medium. In the Soviet Union, as early as 1949, Serebriakov and Khessine demonstrated the importance of brushing teeth with pastes mixed with sodium fluoride; it was experimentally observed that the superficial losses of substance could heal thanks to the action of these pastes, which were active not only at the level of the carious tissues, but also in various lesions of the enamel, due to organic and inorganic acids, since the application carried out with these methods and with a proper brushing carried out directly by the operator allowed an increase in the barrier properties of the enamel and dentin against germs and caries fermentation. Also in the Soviet Union, Lukomsky had used fluoride toothpaste exclusively on the right molars of 148 children aged six to twelve years, while those on the left were deliberately excluded from brushing. After two years, 35 of the untreated teeth were decayed, whereas only one of all the teeth to which the specific treatment had been given had dental decay [Palazzi and Gallinari, 1952].

In Italy, the first experimental studies on the effectiveness of fluoride as a prophylactic means were initiated by the Dental Clinic of the University of Pavia, directed by Silvio Palazzi, in collaboration with Alessandro Seppilli, director of the Institute of Hygiene of the University of Perugia; the research of these two scholars demonstrated the bacteriostatic and antifermentative power of fluoride applied directly to enamel [Seppilli, 1951; Candeli et al., 1952] as well as the preventive and prophylactic power of fluoridated toothpaste (Palazzi and Gallinari, 1952). In 1951 researchers from the Dental Clinic of the University of Pavia and the Institute of Hygiene of the University of Perugia prepared an experimental toothpaste incorporating sodium fluoride at various concentrations, from 0.50% to 1.25%; recently extracted teeth were treated with this compound and it was observed that enamel and dentin showed morphological changes. In 1953 there was an important event at the Dental Clinic of the University of Pavia: the first Symposium on Fluoride. The Fluorine Symposium was proposed at the XXVII Italian Congress of Stomatology (Rome, October 1952) and was held, with the participation of leading Italian and foreign scholars, on March 30th and 31st 1953 at the Library of the Dental Clinic of the University of Pavia. The various communications of the most authoritative Italian and foreign experts definitively sanctioned the importance of fluoride prophylaxis in dental caries, overcoming the inevitable controversy that had begun to spread in those years. In this regard, we recall that some Italian scholars (Fiorentini in 1951 and Tempestini and Albanese in 1952) considered fluorinated toothpaste and topical applications of fluoride to be absolutely ineffective.

Under the presidency of the Athenian Mavrogordato the final motion was approved, which was sent to the International Dental Federation, and which is considered the first guideline on fluoroprophylaxis: The prophylactic action of fluoride in dental caries is mainly due to its action on enamel and dentin, which, by this action, become more resistant to the determining agents of caries, through changes in their histological structure and their chemical composition in which both the organic and mineral parts participate. This prophylactic action can be achieved either by means of drinking water (containing the optimum of one part per million of fluorine) or by means of a water-based system (containing the optimum of one part per million of fluorine) or with the administration of fluorinated foods (fluoridation of table salt) either with the use of toothpaste (containing Na-F at a concentration of not less than 0.50%) or with the local application of solutions of 2% sodium fluoride. That statement had the following signatures: T. J. Mavrogordato (Athens), President, W. Drum (Berlin), R. Frank (Strasbourg), A. Knappwost (Tübingen), W. Perdock (Groningen), F. Piguet (Geneva), H. Schmid-Kunz (Switzerland), S. Palazzi (Pavia), C. Branchini (Pavia), A. Seppilli (Perugia), A. Candeli (Perugia), M. Talenti (Rome), G. Gallinari (Pavia), C. Cocito (Ferrara). The original document, with the final motion, is still kept in the Library of the Department of Dentistry of the University of Pavia. At the end of the Symposium, after the various reports, the following agenda was approved.

- Not to be questioned anymore, in the prophylaxis of caries, the effectiveness of fluorine, either introduced in soluble form by internal means (drinking water, tablets, etc.) or used, always in soluble form (sodium fluoride and potassium fluoride) to brush on the teeth in exact concentration (2%).
- The fluorine ion is chemically fixed in an insoluble form on both the mineral substance and the organic substance.

Consequently, fluorinated toothpastes are useful for caries prophylaxis under the following conditions: that the contact

between the toothpaste and the tooth is not too fleeting; that the toothpaste constantly contains fluoride in the form of soluble salt; that the content of sodium fluoride, potassium in the toothpaste is sufficiently high (0.50%).

Throughout the 1950s and 1960s, the scientific studies and orientations were oriented towards what was established by the above guidelines; in Italy, among others, the School of Pavia, with Resta and Caprioglio, under the direction of Branchini, offered original contributions by conducting long-term experiments on the effectiveness of topical applications of stannous fluoride in the reduction of caries in children [Caprioglio et al., 1967a, 1967b; Resta 1968]. Also in those years, in vitro research was started on the method of ionophoresis, a term used to indicate the passage of ions in the tissues through a difference in electrical potential that accelerates it. In 1962 were obtained the first results (by Schlegel), which were then confirmed, in vivo with success (by Raulo). Further studies (as those by Bergese, Pouezat and Ericsson) provided further critical insights into the greater effectiveness of the use of ionophoretic devices, which had become increasingly sophisticated, compared to simple topical application.

Literature review and brief bibliometric report

Fluoride in dental science is used in many fields (Table 1) and its importance is confirmed by the high number of studies present in indexed Literature. A broad search on Scopus Database has been conducted using the following MeSH terms: TITLE-ABS-KEY (fluoride AND dentistry).

The search strategy included an initial analysis of the results in the specific Scopus sections dedicated to the different document types, thus allowing to highlight the kind of document (articles; conference papers; reviews; book chapters; articles in press; books; editorials; erratum; notes; and conference reviews). No exclusion criteria have been applied in order to provide a whole publications count.

Calculations were performed with a Statistical package (R® version 3.1.3, R Development Core Team, R Foundation for Statistical Computing, Wien, Austria). The results are showed in Figure 1. Regression analysis showed a linear increase of the documents about fluoride over time (R2= 0.753).

Dentistry field	Clinical use
Paediatric dentistry	prevention, chairside and home supplementation; filling material
Dental hygiene	mouthrinse; toothpaste
Dental Materials	Incorporated in many materials for dental use
Restorative dent.	Compomers
Periodontology	mouthrinse; toothpaste
Orthodontics	prevention, supplementation
Endodontics	ingredient of some endodontic cements
Prosthodontics	ingredient of some prosthodontic cements

TABLE 1 Main clinical applications of fluoride in dentistry.

Furthermore, the analysis has been refined with the function "search within results" with the following MeSH terms for each discipline considered in the investigation: paediatric dentistry, dental hygiene, dental materials, restorative dentistry, periodontology, orthodontics, endodontics, prosthodontics.

Today in the literature, more than 3300 documents have been published on fluoride in dentistry when Scopus-indexed journals are considered. This scientific production mainly consist of original articles (2767). Other contributions are conference reviews (329) and conference papers (111). The main part of this type of research (3042 documents) were published in sources that require university/hospitals special access or consultation under payment, whereas 287 documents were available with an open access route. Concerning geographical origin, the major production is located in the United States, with 713 published files. Other countries have remarkable publication production such as United Kingdom (224 documents), Brazil (177), India (117)

Document type	Number of studies	Paediatr dent	Dental hygiene	Dental Mater	Restor dent	Periodontol	Orthod	Endod	Prosthod
Article	2767	855	834	700	489	333	214	209	108
Review	329	132	132	119	106	65	38	43	31
Conference paper	111	32	15	34	25	7	9	5	2
Note	28	6	5	1			2	3	
Editorial	26	4	5	4	1	1	3	2	
Letter	26	2	8	1	1		1		1
Book Chapter	16	6	5	13	10	5	4	7	4
Short Survey	16	3	7	4	1	1		1	1
Conference Review	4	1		1		1			
Book	3	1							
Erratum	2	1		1				1	
Undefined	1		1					1	
Total	3329	1043	1012	878	633	413	271	272	147

TABLE 2 Number of studies published on fluoride in various dental fields such as paediatric dentistry, dental hygiene, dental materials, restorative dentistry, periodontology, orthodontics, endodontics and prosthodontics. Note that the majority of the studies are multidisciplinary and present cross-matter subjects.

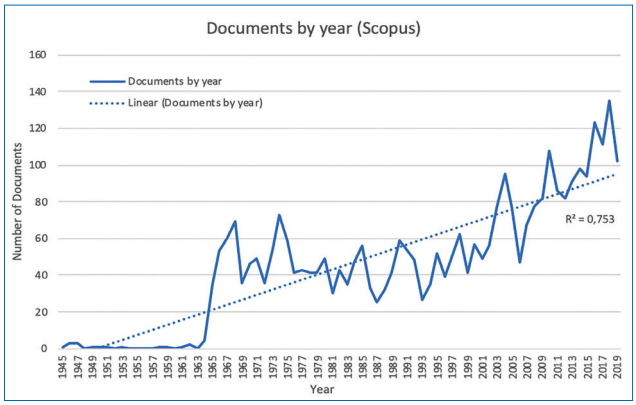

FIG. 1 Number of research papers published on fluoride by year in the field of dentistry (Source: Scopus database).

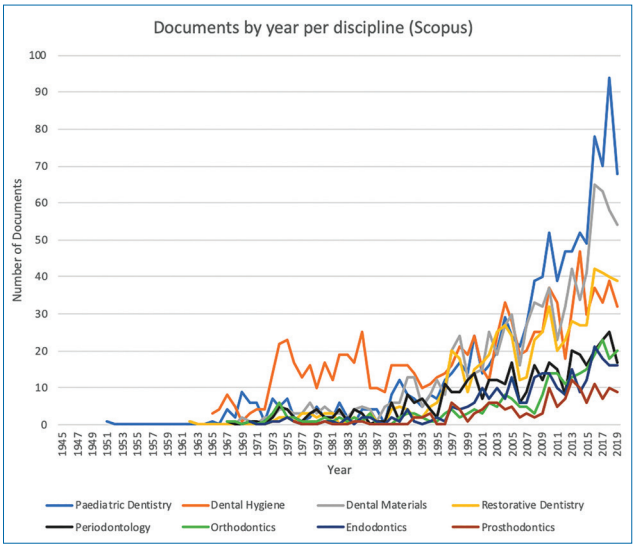

FIG. 2 Number of research papers published on fluoride among the various dental fields (Source: Scopus database).

and Australia (101).

The official Scopus-tracked research on fluoride topic seemed to start in 1945 with a manuscript entitled "Status of fluoride therapy in dentistry" published in Journal of Dental Research [Krasnow, 1945]. The scientific production about this topic remained low (with a maximum of 3-4 published papers per year) until the Sixties. After 1965 an increasing number of studies has been published on the topic, and in 2010 as many as 108 publications in a single year have been reached. The maximum number of studies (134) was published in 2018, thus confirming the great interest about the topic in recent years. Some authors presented a considerable scientific production about fluoride: the most proliphic author is Prof. Herschel S. Horowitz, who published 28 documents about fluoride [Salas-Pereira et al., 2008].

Among various dental fields (Fig. 2), the main area of published material was on paediatric dentistry (855) where 834 documents were about dental hygiene, 700 about dental materials, 489 about restorative dentistry, 333 about periodontology, 214 about orthodontics, 209 about endodontics and 108 about prosthodontics (Table 2). Many studies have a multidisciplinary approach and present cross-matter subjects. Most of the published research was in vitro, but also clinical trials were present with 778 documents.

In paediatric caries prevention, fluoride (Table 1) is used for topic (both chairside and home) and systemic supplementation [Paglia, 2019]. In paediatric and restorative dentistry, it is used as component of compomer filling materials and in fluoride-releasing sealing materials [Khalili Sadrabad et al., 2019]. In fact, the fluoride of these materials cannot prevent the adhesion of streptococcus mutans on restorative materials, however its local cariostatic property significantly reduces demineralization risk [Poggio et al., 2009]. In dental hygiene and periodontology, fluoride is highly used in mouthrinses, toothpastes, gels, remineralising agents and sometimes it covers interdental flosses (Dai et al., 2019 Altinok et al., 2011; Zingler et al., 2016]. In orthodontics, it is a component of many materials used for band cementation [Zingler et al., 2016]. These materials offer excellent mechanical properties [Hung et al., 2019] and bonding efficacy [Paiva et al., 2018]. On the other hand, concerning orthodontic bracket bonding, fluoride adversely affects bond strength [Sfondrini et al., 2010] and its application before bonding would be carefully considered [Scribante et al., 2016]. Finally, fluoride is reported to be present also in some endodontic and prosthodontic materials [Cacciafesta et al., 2005; Kunam et al., 2016].

Future perspectives

The use of fluoride in dentistry sinks its roots in the past and it is linked with future exciting perspectives. New remineralising pastes could help the dental clinician to reduce hypomineralised lesions [Scribante et al., 2020]. The incorporation of fluoride could be tested in other dental materials, such as fiber reinforced composites [Cacciafesta et al., 2005; Giusti et al., 2018; Scribante et al., 2018] or CAD CAM manufactured frameworks [Kunam et al., 2016; Niem et al., 2019]. Moreover, randomised clinical trials about long-term effects of topic and systemic supplementation would be very difficult to realize but could be very useful for clinical practice. Therefore, future in vitro and in vivo reports would be welcome to increase the knowledge about this topic: the research options with fluoride-based materials are open and future reports are expected to increase the awareness during use in the dental field.

Conflict of interest statement
The authors declares that there is no conflict of interest.

Funding
None.

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