



IJCRR
Section: Healthcare
ISI Impact Factor
(2019-20): 1.628
IC Value (2019): 90.81
SJIF (2020) = 7.893

Copyright@IJCRR

Use of Fluoridated Toothpaste in Children - A Review

**Jasmin Winnier¹, Sanjana Kodical², Ashveeta Shetty², Arwa Soni³,
Parnaja Valke³, Miloni Sanghavi³**

¹Associate Professor, Department of Pediatric and Preventive Dentistry D. Y. Patil Deemed to be University School of Dentistry, Navi Mumbai, India; ²Senior Lecturer, Department of Pediatric and Preventive Dentistry, Navi Mumbai, India; ³Postgraduate student Department of Pediatric and Preventive Dentistry, Navi Mumbai, India.

ABSTRACT

Studies have shown that early fluoride use or "low but excessive" fluoride intake during the development of teeth is a risk factor for dental fluorosis in both fluoridated and non-fluoridated environments. Fluorosis affects children under the age of six who have developing, unerupted, and erupted permanent teeth. This changes the appearance of the teeth and leads to mental disturbance. This review enumerates fluoride, fluoridated toothpastes and its utilization in children.

Key Words: Fluoride, Children, Safety, Mechanism, Environments, Enumerates

INTRODUCTION

In the majority of nations, dental caries is a widespread health issue. Caries affects 60% to 90% of children worldwide, and its prevalence varies greatly depending on factors including race, socioeconomic position, the way of life, food habits, and dental hygiene habits.^{1,2}

Dental caries is a multifactorial illness that develops when several elements interact simultaneously in the oral environment, including the host, dietary sugars, and dental biofilm. A half-century ago, the intricate and protracted interplay of these elements and how they result in caries were characterised.¹ If ignored, substantial tooth loss caused by the infection and concomitant conditions can have a negative effect on a child's sleep, eating, physical development, emotional health, and capacity to learn or carry out daily tasks.¹

In light of what we currently know, the most obvious strategy for preventing caries is to manage the root causes by eliminating the tooth biofilm and consuming less sugar. These methods are the foundation of extensive protocols to control the disease, but because they heavily rely on patient compliance, they have been shown to be insufficient to achieve the appropriate degree of prevention. Fluoride had become an essential supplement to treat the condition even before the full aetiology of tooth caries was understood.⁴

Dentifrice with fluoride is a practical at-home method for preventing caries. For more than 50 years, using fluoride toothpaste has been advised (Wright et al., 2014), and the American Academy of Pediatric Dentistry (AAPD) recommends that all kids brush their teeth twice a day with a suitable amount of fluoridated toothpaste (AAPD, 2016). However, consuming too much fluoride can have a number of harmful and adverse effects.

Historical overview of fluoride use

It is not a novel concept to use fluoride as a helpful agent in caries prevention. Black and McKay were the forerunners in this aspect. The observation and documentation of the effects of fluoride began in the late 19th and early 20th centuries.¹ McKay was looking into the brown marks on people's teeth that were common across the USA. It was described as speckled enamel by him. Fluoride was established as the cause of the symptoms in 1931 by Churchill's chemical investigation.¹

Following the discovery, Dean methodically carried out a number of epidemiological investigations and established a association between the amount of enamel spots and content of fluoride, which he called dental fluorosis.¹ He observed a remarkable inverse relationship between the prevalence of dental fluorosis in the USA up until 1942 and the incidence of caries in young people.¹ He concluded his 21-city study

Corresponding Author:

Dr. Aarti Sethia, Assistant professor, Dept of Orthodontics & Orthopaedics D Y Patil University, School of Dentistry, Nerul, Navi Mumbai, India.

ISSN: 2231-2196 (Print)

ISSN: 0975-5241 (Online)

Received: 24.12.2020

Revised: 22.01.2021

Accepted: 23.02.2021

Published: 10.03.2021

by discovering that consuming water with 1 ppm of fluoride can help prevent dental cavities, strengthen teeth, and has no adverse effects on enamel.

In the Grand Rapids, Evanston, Brantford, and Newberg in America, where 1 mg of fluoride per litre was added to drinking water, the first research about beneficial benefits were carried out in 1945. The outcomes were impressive where 50% reduction in dental caries was observed. They arrived to the conclusion that fluoride, at the right quantities, had a considerable effect on dental caries.^{1,2,3,4}

In 1950, Bibby et al. compared, fluoride-coated pills meant to be ingested and fluoride lozenges meant to dissolve gradually in the mouth. The research group that took lozenges demonstrated a reduction in the number of new caries lesions. The notion of systemic fluoride consumption and its absorption into enamel during tooth formation (odontogenesis) was re-examined as a result of the investigations this research sparked comparing pre- and post-eruptive effects.¹ Studies conducted over the past 30 years have revealed that fluoride works best as an anti-caries agent when applied topically and in close contact with the tooth's surface. Regular use of topical supplements containing the right amount of fluoride is advantageous.¹

Fluoride Metabolism

It is the thirteenth most abundant terrestrial substance and makes up 0.06 to 0.09% of the crust's mass. The lithosphere, atmosphere, hydrosphere, and biosphere all contain fluorine. Volcanic rocks contain a significant amount of it. It enters the environment as a result of volcanic, rock erosion, and eruptions a number of human endeavours (coal burning, mineral processing, fertilizers production and consumption, and industrial plants).^{1,2} After intake, about 90% of fluoride is absorbed in the digestive system, moved into the bloodstream, and then dispersed. The final 10% is eliminated by faeces. Children retain fluoride at a rate of about 50%, but adults do so at a rate of about 36%. 99% of fluoride is found in mineralized tissues (such as bone and teeth), whereas 1% is found in soft tissues.¹

Fluoride levels in the mother's bloodstream determine how much fluoride is absorbed by the placenta in pregnant women. Fluoride is transported into the placenta at low concentrations. About 60% of the mother's bloodstream's concentration ends up in the placenta on average. The placenta acts as a barrier to prevent fluoride from entering the foetus, if the quantity rises beyond 0.4 ppm, shielding the foetus from exposure to high fluoride concentrations.^{1,2} Although the concentration is minimal, fluoride can also be passed from the plasma into the mother's milk.¹

What are topical fluorides?

Topical fluorides are typically "A fluoride applied directly to the teeth, especially of children, in a dental caries prevention

program". High quantities of topical fluoride are applied to the dentition's exposed surfaces in order to have a local protective impact and increase the teeth's resistance to decay. Topical fluorides are administered directly to the teeth and work best when given in very small dosages multiple times each day (Ijaz, 2010). The two types of fluorides used topically are self applied and professionally administered. While fluoride gels, foams, and varnishes are normally given to teeth by a dental expert, self-applied therapy includes toothpaste and mouthwash.¹

Mechanism of action of topical fluorides

Fluoride's main and most important effect is topical when the fluoride ion is present in saliva in the right concentration.¹ The primary mineral responsible for constructing permanent tooth enamel when tooth growth is complete is hydroxyapatite.² If the right ions are present in the saliva, the enamel will undergo significant remineralisation activities in addition to multiple demineralization events as the tooth develops. The enamel may become weaker or stronger as a result of these activities. Fluoride inhibits calcium hydroxyapatite's ability to dissolve in an acidic environment. Through a variety of methods, the primary activity is the suppression of enamel demineralization. The most significant cariogenic bacterium found in plaque fluid is *S. mutans*. Lactic acid is produced when bacteria break down carbohydrates, which lowers the pH of saliva. Enamel starts to demineralize and develop caries when the pH drops below the crucial pH for hydroxyapatite (pH 5.5). With the right preventive measures, it is possible to slow the development of new lesions in the early stages of the process. Fluoride will adsorb into the crystal surface of plaque fluid and prevent crystals from dissolving, which will lessen demineralization. If the pH drops below level 5.5, the partial fluoride ion coating will cause the crystal's uncoated portions to dissolve in some areas of the tooth. The increasing level of fluoride ion causes remineralisation when the pH exceeds the crucial value of 5.5 because it enters into the enamel and creates fluorhydroxyapatite. After numerous cycles of demineralization and remineralization, the critical pH level of newly formed crystals may be decreased to 4.5, which may cause the outer layers of enamel to change and become more resistant to the acidic environment. Thus, the processes of demineralization and remineralisation are the most significant effects of fluoride on the advancement of caries.¹

History of toothpastes

By no means are toothpaste and tooth powder recent innovations. Ancient Egyptians created the first dental cream between 3,000 and 5,000 BC that included pumice, myrrh, powdered oxen hoof ashes, and egg shells primarily for cleaning teeth. Water was probably only added if required. Around 1,000 BC, the Persians added gypsum, herbs, honey,

and charred oyster and snail shells. A further 1,000 years later, Romans and Greeks added oyster shells and crushed bones in addition to other abrasives.

Romans appear to have been the first civilization to flavour its paste, possibly to combat halitosis and to make it more palatable. This flavouring was essentially powdered bark and charcoal, which is a distant relative of modern flavours. India and China started employing a powder or paste at about the same period. In particular, the Chinese were using flavourings like herbal mints, ginseng and salt to create toothpastes that were almost similar those currently in use. The most frequent problems with old toothpastes were their increased abrasiveness, bad flavour, and expensive price, which prevented them from being regularly used. Up to the beginning of the industrial era in the 18th century, when toothpowder use increased, not much changed. Toothpowders were created by physicians, dentists, and chemists with the express objective of cleaning teeth. These powders were extremely abrasive to teeth since they contained abrasives including cuttlefish, crushed china, brick dust, and earthenware. For the majority of toothpowders, the still-common sodium bicarbonate served as the body.¹

Unquestionably one of the most significant developments in the history of toothpastes occurred in 1914 with the addition of fluoride. Improvements in or relevant to dentifrices are covered in British Patent GB 3,034 (filed in 1914, patented in 1915), which also includes toothpaste formulations incorporating sodium fluoride among other ingredients. However, it is unknown when the first fluoride toothpaste was effectively available in the market. Crest toothpaste may have been the first fluoride toothpaste to be commercially available anywhere in the world. It was introduced by Procter & Gamble in the USA in test markets in 1955 and across the country in 1956. This launch was preceded by more than 10 years of caries research and was made possible in large part by a collaborative study endeavour directed by Dr. Joseph Muhler at Indiana University. When Bibby examined the anticaries advantages of different toothpastes with sodium fluoride concentrations of 500 ppm fluoride in children and adolescents, he was unable to show a cariostatic benefit.¹ A brand-new toothpaste was created that contains heat-treated calcium phosphate as an abrasive and 1,000 ppm of stannous fluoride as fluoride. A clinical study found that using this toothpaste dramatically decreased the prevalence of dental cavities in children.¹

The American Dental Association (ADA) initially opposed fluoride, which is understandable given the poor knowledge of fluoride's toxicity at the time, therefore the new findings were generally viewed with some scepticism. However, the ADA permitted the use of fluoride salts in toothpastes in 1960, paving the way for their common use. Since the 1980s, fluoride has been an ingredient in almost all com-

mercially available toothpaste formulations in better income countries. Varying fluoride compounds, such as sodium fluoride, sodium monofluorophosphate, amine fluoride, and stannous fluoride, are used both singly and in combination in toothpaste formulations with varying fluoride concentrations. Each manufacturer's requirements for these fluoride compounds' compatibility with other crucial components, especially abrasive systems, must be met (which account for almost half of the entire toothpaste formulation).

Fluoride in Toothpastes

The standard fluoride content of toothpaste is between 1000 and 1500 parts per million (ppm), but toothpaste with higher and lower fluoride contents than usual are easily available in many countries. While there are limitations on the maximum fluoride concentration for toothpaste, there are none on the minimum fluoride concentration. Higher concentrations are often only available by prescription and are hardly available over-the-counter. Patients at high risk for tooth decay in the UK 2800 ppm sodium fluoride toothpaste can be given for people 10 years of age and older, those with caries already present, orthodontic appliances, or those on highly cariogenic diets or medications; patients at high caries risk can also receive it. Patients 16 years of age and older, those with dry mouth, orthodontic appliances, overdentures, or those on highly cariogenic diets or medications, as well as those with present or probable root caries, can be prescribed 5000 ppm toothpaste.¹

Although fluoride toothpaste may provide better defence against dental caries, it also increases the incidence of fluorosis (enamel defects caused by chronic ingestion of excessive amounts of fluoride during the period of tooth formation). Although the amount swallowed varies greatly, chronic fluoride ingestion from toothpaste is common in young children. The younger the child, the more likely it is that they will swallow larger amounts, which frequently make up a significant portion of their daily fluoride intake and can be enough to cause fluorosis.^{1,2,3,4} A threshold of 0.05 mg F/kg to 0.07 mg F/kg body weight has been established, although the exact amount of fluoride (F) consumed beyond which fluorosis may occur is unknown.¹

For a 1-year-old (10 kg) or a 5- to 6-year-old (20 kg), respectively, accidentally eating one- or two-thirds (45 g to 90 g) of a toothpaste tube could be fatal because the probable deadly dose is around 5 mg F/kg body weight (Whitford 1992).¹ For this reason, it is recommended that a fluoride toothpaste should be kept out of the reach of young children.

Why is fluoride a double edge sword?

Additionally, some contend that using fluoride toothpaste in areas where community water is fluoridated provides greater protection than either practise by itself. A significant risk fac-

tor for dental fluorosis, or enamel defects caused by young children consuming excessive amounts of fluoride over time (up to the age of 6), may be the early use of fluoride toothpaste by young children, according to some research. This risk has been linked to an increase in both fluoridated and non-fluoridated communities. (Ellwood 1995; Horowitz 1992;)

Numerous toxicities and negative consequences associated with fluoride overdose can occur. Ullah, Zafar, and Shahani claim that dental fluorosis, which is characterised by hypomineralization of dental enamel and secondary staining, is the earliest and most sensitive sign of chronic fluoride toxicity (2017). Multiple teeth are negatively impacted by severe fluorosis' visual effects, which in turn causes a variety of mental issues.^{1,2}

Ingestion of fluoride-containing tooth paste continues to be the leading cause of fluoride toxicity, followed by the use of fluoride-containing mouthwashes and supplements, according to data on fluoride poisoning compiled by the American Association of Poison Control (AAPC) and other studies.^{1,2,3} More than 80% of the cases of fluoride poisoning reported so far have involved children younger than six.¹

The gastrointestinal tract quickly and almost completely absorbs soluble fluoride molecules like sodium fluoride.¹ The majority of the fluoride in toothpaste that is swallowed is also absorbed, according to recent studies, albeit absorption can be slowed down or lowered by the consumption of food or milk.^{1,2,3,4}

Reasons for increase fluoride uptake / Risks of fluoridated toothpastes in children

The growth in children's use of fluoride toothpaste has been attributed to a number of factors. Kid-friendly flavours added to dentifrices also encourage young children to swallow toothpaste voluntarily, which increases the likelihood that a child will eat a toxic quantity of fluoride because children's swallow mechanisms are not completely developed. Inappropriate toothpaste use is another risk factor because the quantity of toothpaste used during teeth brushing has a big impact on how much fluoride is ingested. (do Nascimento, 2013; Zohoori et al., 2012)., No matter their nationality, the majority of parents had given their kids toothpaste that was too big. 'Children also dispensed a larger amount of toothpaste by themselves^{2,3} A subsequent study, conducted in the United States by Levy and colleagues, confirmed Bentley's findings that parents typically exceed the recommended dose of fluoridated toothpaste.⁴ Basch et al. (2013) found that 90% of toothpaste commercials for preschool children showed misleading amounts that were more than four times the advised amount.⁵

Recommended fluoride level in children

The American Dental Association (ADA) Council on Scientific Affairs met with participants in an April 2012 meeting to

review various public messaging strategies about the usage of fluoride toothpaste for young children. The participants concurred that it would be better and less perplexing for the general public if there was a single advice on the usage of fluoride toothpaste for young children. (2014).⁶

The Council advised a thorough examination of the available data to determine the efficacy and safety of fluoride toothpaste use for young children. The review's findings showed that using fluoride toothpaste can effectively lower caries in children under the age of six. Additionally, it was discovered that consuming amounts equivalent to peas or more can cause minor fluorosis. The ADA now advises caregivers to wash their teeth with water for children under two and to see a dentist or doctor before using fluoride toothpaste. It is recommended to use a pea-sized amount of fluoride toothpaste on children between the ages of 2 and 6.⁷

For children under the age of two, some suggestions suggest using a "smear" of fluoride toothpaste (about 0.1 grams of toothpaste or 0.1 milligrams of fluoride), and for children between the ages of two and six, a pea-sized amount (around 0.25 g toothpaste or 0.25 mg fluoride).⁸

Children are exposed to fluoride through consumption of food and beverages, thus the Council advises using a pea-sized amount of toothpaste for children aged 3 to 6 years after the eruption of the first tooth because of consideration of these additional possible sources of fluoride and the danger of developing fluorosis at the time of tooth formation. This regimen aims to reduce the risk of developing fluorosis while maximising the advantages of fluoride for preventing dental cavities. Therefore the recommended pea sized amount of toothpaste, which ranged from 0.15 to 0.25 g, is supposed to balance the caries-preventive benefits of fluoride with its harmful effects.⁹

	Fluoride concentration of paste in ppm F		
	500 ppm F 0.5 mg F/g	1000 ppm F 1 mg F/g	1500 ppm F 1.5 mg F/g
"Thin smear" 0.125g	0.06 mg	0.13 mg	0.19 mg
"Small Pea" 0.25g	0.13 mg	0.25 mg	0.375 mg
"Half head" 0.5 g	0.25 mg	0.5 mg	0.75 mg
"Full head" 1.0 g	0.5 mg	1.0 mg	1.5 mg

Studies where toothpaste dispense interventions were given

The amount of toothpaste that parents dispensed for their children after the intervention was closer to the recommended amount when compared to the data pooled from earlier studies, where it was observed that all parents gave their children more toothpaste. This finding suggests that when verbal descriptions were combined with visual depictions, the recommended amount was more likely to be achieved.^{10,11}

Colleen E (2011) performed a study to evaluate the amount of toothpaste dispensed by parents, it was observed that parents usually use more toothpaste on their young children than is advised for fluoridated toothpaste for youngsters. Their test of verbal instructions to parents to limit the amount to a “smear” or a “pea size” amount did not result in the recommended amounts, their findings suggest there is some value in instruction, but that verbal instruction alone is not enough and the use of visual aids and demonstration are recommended as strategies to further improve parent education.

Guidelines of the American Academy of Pediatric Dentistry (AAPD)

Current guidelines of the American Academy of Pediatric Dentistry (AAPD) recommend teaching caregivers to use a “smear” of fluoridated toothpaste for children younger than two years old at moderate or high caries risk and a “pea-sized” amount for all children age two through five years.² Although the AAPD provides images that depict these amounts as a point of reference, it might be challenging to determine the depth of the toothpaste exhibited on the toothbrush, and the recommendations don’t include any additional clues like the ideal weight or length of the quantity of toothpaste. Reliance on parents’ understanding of the verbal labels “pea” and “smear” could lead either to over- or under-dosing of fluoridated toothpaste

Young children and fluoride importance

Because the deciduous dentition is present while the permanent dentition is forming, young children are more vulnerable, and fluoride exposure can impede the process.¹² Young children have less coordination and comprehension than adults, which makes it more likely that they would swallow the dentifrice rather than expel it after brushing. This increases the risk of fluorosis.¹³⁻¹⁶

Studies have also revealed that the majority of the ingested fluoride may be absorbed, primarily from the small intestine, if absorption is not hindered by the presence of other metal ions.¹⁷⁻²²

Adverse effects of fluoride from oral care regimens

Review of the research on the negative effects of fluoride from oral care practises and treatments,²³ Enamel fluorosis has been linked in a substantial way to fluoride in dental care products.²⁴

Toothpastes and fluorosis

Additionally, roughly 95% of all dentifrice use is fluoride-based. As a result, the logical notion that fluoride dentifrice may play a role in increasing the risk of fluorosis has emerged, and it has been examined by a number of research-

ers.^{25,26} Osuji et al. (1988) showed a clear correlation between early usage of fluoride toothpaste and increased incidence of dental fluorosis in a community treated at 1 ppm.¹

Holt and Murray (1997) postulated 7 issues pertaining to fluoride in toothpastes, out of that 5 are either directly or indirectly related to the risk of developing fluorosis.

CONCLUSION

Parents have to be adequately educated about the benefits, usage and adverse effects of fluoridated toothpastes

ACKNOWLEDGEMENT

I acknowledge the scholars whose articles are included in references to this manuscript. I am also thankful to the authors/editors/publishers of those articles and journals from where the literature for this article has been reviewed. I am extremely thankful to the editorial board of “International Journal of Current Research and Review” who have helped in the publication of this manuscript.

Source of Funding: NIL

Conflict of Interest: NIL

REFERENCES

1. Petersen PE, Bourgeois D, Ogawa H, Estupinan-Day S, Ndiaye C. The global burden of oral diseases and risks to oral health. Bull World Health Organ. 2005 Sep;83(9):661-9. Epub 2005 Sep 30. PMID: 16211157; PMCID: PMC2626328.
2. Anil S, Anand PS. Early Childhood Caries: Prevalence, Risk Factors, and Prevention. Front Pediatr. 2017 Jul 18;5:157.
3. Keyes PH: The infectious and transmissible nature of experimental dental caries: findings and implications. Arch Oral Biol 1960;1:304–320.)
4. Cabral MBBS, Mota ELA, Cangussu MCT, Vianna MIP, Floriano FR. Risk factors for caries-free time: longitudinal study in early childhood. Rev Saude Publica. 2017 Dec 4;51:118.
5. Black GV, McKay FS. Original Communications. Mottled teeth: an endemic developmental imperfection of the enamel of the teeth heretofore unknown in the literature of dentistry. Dental Cosmos. 1916;58:129–56.
6. Churchill HV to McKay FS. Jan. 20, 1931, in the ALCOA (Aluminum Company of America) papers Churchill HV. Occurrence of fluorides in some waters of the United States. J Ind Eng Chem. 1931;23:996–
7. Dean, H. T., Dixon, R. M., and Cohen, C. Mottled Enamel in Texas. Pub. Health Rep., SO: 424-442 (Mar. 29), 1935
8. Dean HT. Classification of mottled enamel diagnosis. J Am Dent Assoc. 1934;21:1421–6.
9. Arnold FA, Jr, Likins RC, Russell AL, Scott DB. Fifteenth year of the Grand Rapids fluoridation study. J Am Dent Assoc. 1962;65:780–85
10. Blayney JR, Hill IN. Fluorine and dental caries. J Am Dent Assoc. 1967;74:225–302.

11. Hutton WL, Linscott BW, Williams DB. Final report of local studies on water fluoridation in Brantford. *Can J Public Health*. 1956;47:89–92.
12. Ast DB, Fitzgerald B. Effectiveness of water fluoridation. *J Am Dent Assoc*. 1962;65:581–7
13. Bibby BG, Wilkins E, Witol E. A preliminary study of the effects of fluoride lozenges and pills on dental caries. *Oral Surg Oral Med Oral Pathol*. 1955;8(2):213–6
14. Petersen PE, Lennon MA. Effective use of fluorides for the prevention of dental caries in the 21st century: the WHO approach. *Community Dent Oral Epidemiol*. 2004;32:319–21.
15. Fawell J, Bailey K, Chilton J, Dahi E, Fewtrell L, Magara Y. Fluoride in drinking-water. London: World Health Organization (WHO); 2006. [Access: March 16 2015].
16. Australian Government. National Health and Medical Research Council. A systematic review of the efficacy and safety of fluoridation. PART A: review of methodology and results. 2007. [Access: March 18 2015]
17. Buzalaf MA, Whitford GM. Fluoride metabolism. *Monogr Oral Sci*. 2011;22:20–36. Doi: 10.1159/000325107. 15)
18. GS M, Mohanty S, Rao P. Role of placenta to combat fluorosis (in fetus) in endemic fluorosis area. *NJIRM*. 2010;1(4):16–19.
19. Gupta S, Seth AK, Gupta A, Gavane AG. Transplacental passage of fluorides. *J Pediatr*. 1993;123:139–41.
20. Ekstrand J, Boréus LO, de Chateau P. No evidence of transfer of fluoride from plasma to breast milk. *Br Med J. (Clin Res Ed.)* 1981;283:761–2.)
21. American Dental Association. Fluoridation Facts. Chicago, IL. Available from http://www.ada.org/sections/professionalresources/pdfs/fluoridation_facts.pdf. [Last accessed on 16 November 2016]
22. Buzalaf MA, Pessan JP, Honório HM, ten Cate JM. Mechanisms of action of fluoride for caries control. *Monogr Oral Sci*. 2011;22:97–114
23. Fincham AG, Moradian-Oldak J, Simmer JP. The structural biology of the developing dental enamel matrix. *Journal of Structural Biology*. 1999;126:270–99).
24. Buzalaf MA, Pessan JP, Honório HM, ten Cate JM. Mechanisms of action of fluoride for caries control. *Monogr Oral Sci*. 2011;22:97–114. Doi: 10.1159/00032515133)
25. Lippert F. An introduction to toothpaste - its purpose, history and ingredients. *Monogr Oral Sci*. 2013;23:1-14}
26. Bibby BG: A test of the effect of fluoride containing dentifrices on dental caries. *J Dent Res* 1945;24:297–303.