

## Fluoride Concentration in Toothpastes Marketed in Pakistan

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**Summary:** Efficacy of fluoride as a cariostatic agent is a well-established fact. Last few decades have seen a dramatic decline in dental decay throughout the world. As a systematic approach, fluoride is added to the drinking water to prevent dental decay but topical application using toothpaste has been more effective against dental caries, therefore fluoride is added to toothpaste in the form of sodium fluoride and sodium monofluorophosphate. Based on the fact that excessive exposure to fluoride causes dental fluorosis and lower amount makes toothpaste ineffective against dental caries, so the amount of fluoride in the toothpaste must be regulated. Therefore, in the present study, toothpastes including local and imported brands sold in Karachi have been collected and analyzed for their fluoride contents. In a total of 55 samples, amount of fluoride ranged from 10 to 1,674 ppm in local samples and in imported brands it ranged from 426 to 1,444 ppm. Eighty-two percent of the local brands fell short of 1,000 ppm fluoride which is the lower limit of fluoride in toothpaste as recommended by WHO. A large amount of variations has been observed in acclaimed fluoride levels and analyzed fluoride level; furthermore, 70% of the local samples have not even mentioned the content of fluoride in their brands. In the context of increasing number of cases of dental decay in Karachi, these results provide baseline data to the authorities concerned to regulate the fluoride levels in toothpaste.

**Keywords:** Dental decay, Dental fluorosis, Fluoride toothpastes, Karachi.

### Introduction

Fluoride, being the 13<sup>th</sup> most abundant element on earth [1, 2] and present in different forms in the environment including edible items, drugs and drinks [3], therefore, human beings constantly come into contact with it. A controlled amount of fluoride is amiable for the body but an excess may lead to certain health problems [4]. An excessive fluoride intake causes fluorosis in teeth and bones [5]. Fluoride is very useful in preventing dental caries and past few years have seen a decline in dental caries [6-10] but a simultaneous rise in fluorosis is also observed [11]. Rise in fluorosis may be a cause of the excess use of fluoride in the drinking water and dentifrice containing fluoride [12]. In many countries fluoride is added in water, toothpaste and other dentifrices to supplement its deficiency [13-15]. Use of fluoride-containing toothpaste before the age of 6 years increases the risk of fluorosis in individuals [11].

Dental decay has been a severe problem throughout the world and also in Pakistan [16-21]. Bacteria like streptococci metabolize the fermentable carbohydrates from the diet and release acids [22-24]. These acids then start demineralization of tooth enamel which is made of hydroxyapatite calcium phosphate and is soluble in the acidic environment [21]. Fluoride helps in demineralization of dental enamel by being adsorbed at the tooth enamel surface

and thus decreasing its solubility in acids [21]. Fluoride not only inhibits the demineralization of enamel, but it can also reverse it or remineralize it by producing a new crystalline surface of fluoroapatite nature which has a much lower solubility in the acids [21, 25]. Several studies have also indicated that fluoride interferes with bacterial activity in the form of HF formed in the acidic conditions provided by the acidogenic bacteria, thus debilitating their activity [21, 26, 27].

The amount of fluoride in drinking water is typically much lower to be effective against dental caries process. In different parts of the world, fluoride is added to drinking water to control dental caries, but studies have shown that topical application of fluoride on teeth in the form of toothpaste is responsible against dental decay [28, 29]. Furthermore, a high amount of fluoride in drinking water is a cause of concern as it may lead to dental fluorosis. This necessitates the use of fluoride in dentifrice as topical application [30, 31].

Several types of toothpaste are sold in Pakistani market including local as well as imported brands having a varying amount of fluoride in the form of sodium monofluorophosphate (MFP) and sodium fluoride. Some toothpastes are labeled double fluoride which contains both MFP and sodium fluoride, however, some contains only one of them.

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Apart from sodium fluoride and MFP, amine fluoride and stannous fluoride have also been used in toothpastes as therapeutic agents for caries control but these have received a little acceptance. Amount of fluoride in toothpastes typically ranges from 700 to 1,500 ppm, however, the optimum amount of fluoride in toothpaste is based on the level of fluoride exposure in a region from all sources. According to the Scientific Committee on Cosmetic Products and Non-Food Products (SCCNFP), if toothpaste is the only source of fluoride exposure then, fluoride levels of 1,000-1,500 ppm are the permitted range to be cariostatically effective and avoiding dental fluorosis as well, especially for the children under age of 6 years. It also recommends a pea sized (quarter of a brush size) amount of toothpaste for the children under 6 years of age [32].

In the current study toothpaste sold in the Pakistani markets have been analyzed for their fluoride contents to ensure that their claim for the amount of fluoride is justified. Since some local brands only mention fluoride in their labels but do not mention the amount and form of fluoride in the product, therefore it is necessary to analyze them for their fluoride composition.

## Experimental

### *Fluoride Toothpaste Samples*

A total of 55 toothpaste samples of different brands those claiming fluoride in their formulation (except 2 samples) were bought from different sites of the local market of Karachi. Out of which 33 were local brands, whereas remaining were of imported brands from various countries. Therefore, all the samples were classified into two main groups namely Local Brand (LB) and Imported Brand (IB).

### *Fluoride Declaration*

The packages of the toothpastes were checked to see the information regarding the forms of fluoride contents and their claimed concentration. On the packaging of the toothpaste the quantity of fluoride was specified in ppm units or the percentage. However, percentage, where mentioned, was converted into ppm unit to unify the calculations.

### *Set-Up*

Accurately 0.5 g of each toothpaste sample was weighed, homogenized in 10 mL of deionized water followed by addition of 5 mL of 2.0 M HCl and kept at 45°C for an hour to ensure complete digestion of all form of fluoride in the toothpaste matrix. [33, 34]. The samples were then neutralized

with 1M NH<sub>4</sub>OH and filtered to avoid any insoluble particles. Afterwards, 50 mL of the TISAB (total ionic strength adjusting buffer) solution was added and the sample was then made up to 100 mL with deionized water. A 50 mL of the clear solution was taken in a beaker and analyzed for fluoride by fluoride ion selective electrode (FISE) which was previously calibrated using fluoride standards. FISE was used to measure fluoride content in the digested samples because of its sensitivity, selectivity, rapidity and an adequate limit of detection.

## Results and Discussion

Summary of results of all the 55 samples of toothpaste are given in Table-1 and fluoride levels in imported brands of toothpastes and those of local brands have been shown separately in Tables-2 and 3 respectively. There are 33 samples of local brands while 22 samples are imported brands. 10 out of the total 55 samples are kid's toothpastes out of which 7 samples are imported brands and 3 samples are locally manufactured. There are also three samples which are specific for smokers, one of them is local and other two are imported brands. Range of the fluoride contents in the local brands has been found to be 18 to 1,674 ppm and in the imported brands the range is found to be 10 to 1,444 ppm. There was only one local sample that contained fluoride level in excess of 1,500 ppm ( i.e. 1,674 ppm) which is the upper limit of the recommended fluoride levels in toothpastes, however, 82% of the local samples fell short of the lower limit of 1,000 ppm fluoride [32, 34]. Fluoride levels in the range of 1,000 to 1,500 ppm are effective for preventing dental caries without threatening to cause dental fluorosis. But only 6 samples out of 33 local brands and merely 7 samples out of 22 imported brands fall within this range. Only two samples have shown the fluoride content of less than 20 ppm, one of which is Chinese brand herbal toothpaste and other is purely medicinal toothpaste. 34 out of the total 55 samples and most of them being the local ones (70%) do not mention the amount of fluoride in their product (Fig. 1). Only 17 out of the total 55 toothpastes have shown the list of ingredients with their amounts and most of them claim the use of calcium-containing abrasives either in the calcium carbonate or in DCPD (dicalcium phosphate dihydrate) form. Very few have been found to contain both, calcium as well as silica- based abrasives. In the results, a large amount of variation can be seen from the acclaimed fluoride levels in the toothpastes as shown in Fig. 2. These variations are quite higher in the local toothpaste as compared to the imported ones (Fig. 3).

Table-1: Summary of results of fluoride analysis in all the 55 samples of toothpaste.

Description	Local brands	Imported brands
Total number of toothpastes	33	22
Min	18	10
Max	1674	1444
Number of toothpaste below 1000 ppm	27 (82%)	15 (68%)
Number of toothpaste above 1500 ppm	1	0
Number of toothpaste containing Ca <sup>++</sup>	11 (33%)	6 (27%)
Number of toothpaste without fluoride specification	23 (70%)	11 (50%)

Table-2: Results of fluoride analysis (mg/kg) in toothpaste samples of local brand.

S.No.	Sample ID	Type	Make	Calculated Fluoride	Reported Fluoride	% Difference
1	LB-02	Medicinal	Pakistan	18	N/R	N/A
2	LB-31	Kids	Pakistan	169	N/R	N/A
3	LB-30	Kids	Pakistan	426	528	19.32
4	LB-22		Pakistan	514	1400	63.29
5	LB-23		Pakistan	551	N/R	N/A
6	LB-21		Pakistan	645	1400	53.94
7	LB-28		Pakistan	718	1000	28.23
8	LB-14		Pakistan	765	1000	23.52
9	LB-12		Pakistan	766	N/R	N/A
10	LB-13		Pakistan	769	N/R	N/A
11	LB-09		Pakistan	785	N/R	N/A
12	LB-16		Pakistan	793	N/R	N/A
13	LB-06		Pakistan	819	1000	18.12
14	LB-19		Pakistan	822	N/R	N/A
15	LB-29	Smoker	Pakistan	824	1055	21.90
16	LB-05		Pakistan	827	N/R	N/A
17	LB-15		Pakistan	849	N/R	N/A
18	LB-17		Pakistan	860	N/R	N/A
19	LB-24		Pakistan	875	1000	12.50
20	LB-18		Pakistan	906	N/R	N/A
21	LB-03		Pakistan	931	N/R	N/A
22	LB-25		Pakistan	955	N/R	N/A
23	LB-08		Pakistan	957	N/R	N/A
24	LB-32	Kids	Pakistan	967	N/R	N/A
25	LB-11		Pakistan	974	N/R	N/A
26	LB-26		Pakistan	976	N/R	N/A
27	LB-20		Pakistan	989	N/R	N/A
28	LB-33		Pakistan	1099	N/R	N/A
29	LB-01		Pakistan	1181	1450	18.55
30	LB-07		Pakistan	1212	N/R	N/A
31	LB-10		Pakistan	1230	N/R	N/A
32	LB-04		Pakistan	1249	N/R	N/A
33	LB-27		Pakistan	1674	1500	-11.59

N/R = Not reported

N/A = Not Applicable

Table-3: Results of fluoride analysis (mg/kg) in toothpaste samples of imported brand.

S. No.	Sample ID	Type	Make	Calculated Fluoride	Reported Fluoride	% Difference
1	IB-34	Herbal	China	10	N/R	N/A
2	IB-19	Kids	Indonesia	426	N/R	N/A
3	IB-18	Kids	Thailand	436	500	12.89
4	IB-17	Kids	Indonesia	443	N/R	N/A
5	IB-20	Kids	Germany	444	N/R	N/A
6	IB-16	Kids	Indonesia	463	N/R	N/A
7	IB-12	Smoker	Indonesia	678	1055	35.73
8	IB-11		Malaysia	848	1000	15.20
9	IB-15	Kids	England	876	N/R	N/A
10	IB-02		Thailand	897	1000	10.33
11	IB-06			929	N/R	N/A
12	IB-35		UAE	934	N/R	N/A
13	IB-05		Thailand	939	1000	6.08
14	IB-14	Kids	UK	972	1100	11.67
15	IB-13	Smoker	England	988	1100	10.20
16	IB-03		S. Africa	1014	N/R	N/A
17	IB-09		Indonesia	1231	N/R	N/A
18	IB-08		Egypt	1315	1450	9.31
19	IB-07		Indonesia	1330	N/R	N/A
20	IB-01		UK	1385	1450	4.45
21	IB-10		Germany	1412	1450	2.60
22	IB-04		EU	1444	1400	-3.13

N/R = Not reported

N/A = Not Applicable

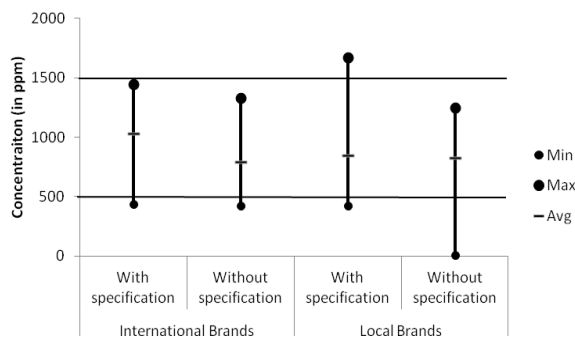


Fig. 1: Samples of Toothpaste with and without specifications.

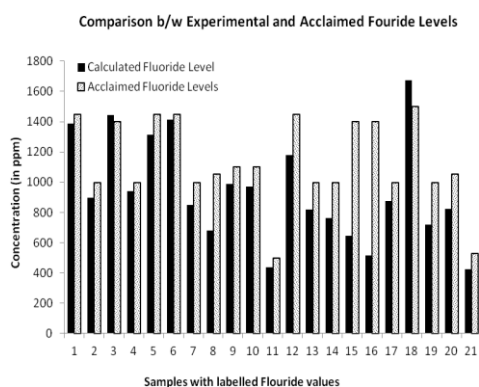


Fig. 2: Comparison b/w experimental and acclaimed fluoride levels.



Fig. 3: Percentage of samples varying from acclaimed fluoride levels.

Keeping in mind the importance of dentifrices as fluoride sources and their possible effects on human health, it becomes extremely important that fluoride levels in toothpastes be regulated according to the total fluoride exposure to the local population of an area. No such regulations regarding fluoride exposure from toothpastes exist in Karachi and other parts of Pakistan. An excess of fluoride causes dental fluorosis and its absence puts oral health in a vulnerable condition against dental caries. According to WHO and European Commission, fluoride levels in toothpaste should be

in the range of 1,000 to 1,500 ppm. This range, besides being cariostatically effective, is regarded safe against dental fluorosis for any age if sole source of fluoride is toothpaste. Furthermore, toothpastes with a fluoride level of 1,500 ppm have been reported to be more effective against dental caries than toothpastes containing 1,000 ppm fluoride [33, 35, 36]. Since the most important source of fluoride exposure is drinking water and the fluoride concentration in drinking water resources of Karachi is very low [37], therefore, for effective controlling of increasing incidences of dental decay, it becomes necessary to meet the regulation limit of fluoride levels in toothpaste. In this study it has been found that 82 % of the local brands and 68% of the imported brand of toothpastes contain fluoride levels lower than 1,000 ppm, which may lead to the increasing number of dental decay cases in Karachi and other parts of Pakistan [19, 38, 39]. Formulation of fluoride in toothpaste plays an important role for it to be effective against dental caries. This is because different formulations have different availability of soluble fluoride in the toothpaste [40]. As the results have shown, 70% of the local samples and 50% of the imported brands do not show the amount of fluoride in their product. Since in most of the samples MFP is used as fluoridating agent, therefore DCPD has been found as an abrasive which is compatible with MFP form of fluoride. This combination of MFP and DCPD has been reported to be more effective against enamel instability as compared to silica-based abrasive containing toothpastes [41]. However, long-term storage of the toothpaste containing DCPD or  $\text{CaCO}_3$  as abrasives reduces the available fluoride in toothpaste. It is also reported that as much as one-third of the total fluoride may be lost during storage by formation of insoluble fluoride with calcium [33, 42, 43]. This makes it necessary for the manufacturer to reveal the fluoride specification in their brands. In our results, only 17 out of the total 55 samples have mentioned the type of abrasive and the form of fluoride on their packaging. Furthermore, analyzed values of fluoride vary from the acclaimed values in the range of -3% to almost 13 % in imported brands. This variation is found to be very high in the local brands ranging from -15% to 63% (Fig 3). One of the toothpaste brand claims fluoride levels to be 1,400 ppm but the experimental value is found to be 514 ppm. These variations show that the fluoride levels are less than those mentioned on the packaging which further decreases the fluoride levels from the recommended levels.

## Conclusions

From results of the study, it could be

concluded that a wide range of variation exists in the fluoride concentrations in toothpastes. Keeping in mind the importance of toothpastes in preventing the dental decays, the authorities concerning the dental health should regulate the toothpaste compositions to effectively control increasing problem of dental decay in Karachi and other parts of Pakistan. Furthermore, toothpaste manufacturing companies should be bound to disclose amount and the nature of fluoride along with the type of abrasives used in their product.

*Conflict of interest: The Authors Declare No Conflict of Interest*

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### References

1. F. M. Fordyce, K. Vrana, E. Zhovinsky, V. Povoroznuk, G. Toth, B.C. Hope, U. Iljinsky, J. Baker, A Health Risk Assessment for Fluoride in Central Europe, *Environ Geochem Health*, **29** 83-102 (2007).
2. R. E. Krebs, *The History and Use of our Earth's Chemical Elements: a Reference Guide*, Greenwood Publishing Group, 2006.
3. J. K. Fawell, *Fluoride in Drinking Water*, World Health Organization, 2006.
4. S. Tokalioglu, S. Kartal and U. Sahin, Determination of Fluoride in Various Samples and Some Infusions Using a Fluoride Selective Electrode, *Turkish Journal of Chemistry*, **28** 203, (2009).
5. A. K. Yadav, C. P. Kaushik, A. K. Haritash, B. Singh, S. P. Raghuvanshi and A. Kansal, Determination of Exposure and Probable Ingestion of Fluoride Through Tea, Toothpaste, Tobacco and Pan Masala, *Journal of hazardous materials*, **142**, 77 (2007).
6. M. Bonecker, P. Cleaton-Jones, Trends in Dental Caries in Latin American and Caribbean 5-6 and 11-13 Years Old Children: a Systematic Review, *Community Dentistry and Oral Epidemiology*, **31** 152, (2003).
7. D. Bratthall, G. HÃ¶nnselÃ¶• Petersson, H. Sundberg, Reasons for the Caries Decline: What do the Experts Believe?, *European Journal of Oral Sciences*, **104**, 416, (1996).
8. T. M. Marthaler, Changes in Dental Caries 1953-2003, *Caries Research*, **38** 173, (2004).
9. E. P. S. Tagliaferro, M. C. Meneghim, G. M. B. Ambrosano, A. C. Pereira, S. H. C. Sales-Peres, A. Sales-Peres, J. R. M. Bastos, Distribution and Prevalence of Dental Caries in Bauru, Brazil, 1976-2006, *International Dental Journal*, **58**, 75 (2008).
10. J. A. Cury, L. M. A. Tenuta, C. C. C. Ribeiro, A. F. Paes Leme, The Importance of Fluoride Dentifrices to the Current Dental Caries Prevalence in Brazil, *Brazilian Dental Journal*, **15**, 167 (2004).
11. A. K. Mascarenhas, B. A. Burt, Fluorosis Risk from Early Exposure to Fluoride Toothpaste, *Community Dentistry and Oral Epidemiology*, **26**, 241 (1998).
12. F. Rojas-Sanchez, S. A. Kelly, K. M. Drake, G. J. Eckert, G. K. Stookey and A. J. Dunipace, Fluoride Intake from Foods, Beverages and Dentifrice by Young Children in Communities with Negligibly and Optimally Fluoridated Water: a Pilot Study, *Community Dentistry and Oral Epidemiology*, **27**, 288, (1999).
13. L. W. Ripa, A Half - Century of Community Water Fluoridation in the United States: Review and Commentary, *Journal of Public Health Dentistry*, **53**, 17 (1993).
14. M. S. McDonagh, P. F. Whiting, P. M. Wilson, A. J. Sutton, I. Chestnutt, J. Cooper, K. Misso, M. Bradley, E. Treasure, J. Kleijnen, Systematic Review of Water Fluoridation, *BMJ*, **321**, 855 (2000).
15. A. J. Spencer, G. D. Slade, M. Davies, Water Fluoridation in Australia, *Community Dental Health*, **13** 27 (1996).
16. R. Maher, A. Khan, S. Rahimtoola, D. Bratthall, Prevalence of Mutans Streptococci and Dental Caries in Pakistani Children, *JPMA J. Pak. Med. Assoc.*, (1992).
17. J. Moses, B. N. Rangeeth, D. Gurunathan, Prevalence of Dental Caries, Socio-Economic Status and Treatment Needs Among 5 to 15 Year Old School Going Children of Chidambaram, *Journal of Clinical and Diagnostic Research*, **5**, 146 (2011).
18. S. Sufia, S. Chaudhry, F. Izhar, A. Syed, B. A. Q. Mirza, A. A. Khan, Dental Caries Experience in Preschool Children--Is It Related to A Child's Place of Residence and Family Income?, *Oral Health & Preventive Dentistry*, **9**, 375 (2011).
19. N. Dawani, N. Nisar, N. Khan, S. Syed, N. Tanweer, Prevalence and Factors Related to Dental Caries Among Pre-School Children of Saddar Town, Karachi, Pakistan: a Cross-Sectional Study, *BMC Oral Health*, **12**, 59 (2012).

20. F. Vakani, N. Basaria, S. Katpar, Oral Hygiene KAP Assessment and DMFT Scoring Among Children Aged 11-12 Years in an Urban School of Karachi, *Journal of the College of Physicians and Surgeons Pakistan*, **21**, 223 (2011).
21. J. D. B. Featherstone, Prevention and Reversal of Dental Caries: Role of Low Level Fluoride, *Community Dentistry and Oral Epidemiology*, **27**, 31 (1999).
22. N. Tinanoff, M. J. Kanellis, C. M. Vargas, Current Understanding of the Epidemiology, Mechanisms, and Prevention of Dental Caries in Preschool Children, *Pediatric Dentistry*, **24**, 543 (2002).
23. R. Touger-Decker, C. Van Loveren, Sugars and Dental Caries, *The American Journal of Clinical Nutrition*, **78** 881S (2003).
24. W. K. Seow, Biological Mechanisms of Early Childhood Caries, *Community Dentistry and Oral Epidemiology*, **26** 8, (1998).
25. J. M. T. Cate, Review on Fluoride, with Special Emphasis on Calcium Fluoride Mechanisms in Caries Prevention, *European Journal of Oral Sciences*, **105**, 461 (1997).
26. R. H. Selwitz, A. I. Ismail, N. B. Pitts, Dental Caries, *The Lancet*, 369, **51** (2007).
27. A. Wiegand, W. Buchalla and T. Attin, Review on Fluoride-Releasing Restorative Materials-Fluoride Release and Uptake Characteristics, Antibacterial Activity and Influence on Caries Formation, *Dental Materials*, **23**, 343 (2007).
28. J. A. Cury, L. M. A. Tenuta, How to Maintain a Cariostatic Fluoride Concentration in the Oral Environment, *Advances in Dental Research*, **20**, 13 (2008).
29. A. Wiegand, T. Attin, Influence of Fluoride on the Prevention of Erosive Lesions--a review, *Oral Health & Preventive Dentistry*, **1**, 245 (2003).
30. E. Hellwig, A. M. Lennon, Systemic Versus Topical Fluoride, *Caries Research*, **38**, 258 (2004).
31. B. A. Burt, The Case for Eliminating the Use of Dietary Fluoride Supplements for Young Children, *Journal of Public Health Dentistry*, **59**, 269 (1999).
32. M. Borremans, J. Van Loco, P. Van Den Meerssche, J. Meunier, E. Vriendts, L. Goeyens, Analysis of Fluoride in Toothpastes on the Belgian Market, *International Journal of Cosmetic Science*, **30**, 145 (2008).
33. J. A. Cury, M. J. L. de Oliveira, C. C. Martins, L. M. A. Tenuta, S. M. Paiva, Available Fluoride in Toothpastes used by Brazilian Children, *Brazilian Dental Journal*, **21**, 396 (2010).
34. O. Adejumo, O. George-Taylor, A. Kolapo, A. Olubamiwa, R. Fayokun, O. Alawode, Determination of Fluoride Concentration in Various Brands of Toothpaste Marketed in Nigeria Using Ion Selective Electrode Method, *Advances in Medical and Dental Sciences*, **3**, 45 (2009).
35. S. Twetman, S. Axelsson, H. Dahlgren, A. K. Holm, C. Kallestal, F. Lagerlof, P. Lingstrom, I. Mejare, G. Nordenram, A. Norlund, L. G. Petersson, B. Soder, Caries-Preventive Effect of Fluoride Toothpaste: a Systematic Review, *Acta Odontologica Scandinavica*, **61**, 347 (2003).
36. G. Rasines, Fluoride Toothpaste Prevents Caries in Children and Adolescents at Fluoride Concentrations of 1000 ppm and above, *Evidence-Based Dentistry*, **11**, 6 (2010).
37. A. Siddique, M. Mumtaz, S. Saied, Z. Karim, N. A. Zaigham, Fluoride Concentration in Drinking Water of Karachi City (Pakistan), *Environmental Monitoring and Assessment*, **120**, 177 (2006).
38. R. Maher, Dental Disorders in Pakistan-A National Pathfinder Study, *J Pak Med Assoc*, **41**, 250 (1991).
39. M. Ali Leghari, F. Tanwir, H. Ali, Dental Caries Prevalence and Risk Factors Among School Children Age 12-15 Years in Malir, Karachi, *Pakistan Oral & Dental Journal*, **32**, 484 (2012).
40. G. K. Stookey, P. F. DePaola, J. D. B. Featherstone, O. Fejerskov, I. J. Moller, S. Rotberg, K. W. Stephen, J. S. Wefel, A Critical Review of the Relative Anticaries Efficacy of Sodium Fluoride and Sodium Monofluorophosphate Dentifrices, *Caries Research*, **27**, 337 (1993).
41. A. Gaffar, J. Blake-Haskins, J. Mellberg, In Vivo Studies with a Dicalcium Phosphate Dihydrate/MFP System for Caries Prevention, *International Dental Journal*, **43**, 81 (1993).
42. L. N. Hashizume, Y. B. de Oliveira Lima, Y. Kawaguchi, J. A. Cury, Fluoride Availability and Stability of Japanese Dentifrices, *Journal of Oral Science*, **45**, 193 (2003).
43. A. S. Chan, Fluoride Stability in Dicalcium Phosphate Dihydrate Composition, in, US, Patent No. 5037636, 6 Aug, 1991