Research Square

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Total, soluble, and ionized fluoride concentration in cavity protection dentifrices marketed in Iran by two analytical methods

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Abstract

Background and Objectives

: Given the proven role of fluoride-containing toothpastes in preventing and controlling dental caries, the present study aimed to determine the concentration of total, soluble, and ionized fluoride in children's and adult toothpastes available in the Iranian market using two measurement methods, including spectrophotometry and potentiometry.

Materials and Methods

In this experimental-laboratory study, the concentration of total, soluble, and ionized fluoride was measured at the beginning and end of two toothpaste tubes from 28 different brands of children's and adult toothpastes available in the Iranian market. The selected products had a production date difference of less than six months and had at least one year until the expiration date. Fluoride measurement was performed using two analytical methods, including spectrophotometry and potentiometry. In addition, parametric and nonparametric statistical tests were used to analyze the data.

Results

The average total fluoride concentration of toothpastes ranged from 552.39 to 3749.41 ppm, and the soluble fluoride concentration ranged from 220.38 to 3436.79 ppm. In all cases, there was no significant difference between the total and soluble fluoride values, or between the soluble and ionized fluoride values ($P > 0.05$), but in 75% of the toothpastes, a significant difference was observed between the total and ionized fluoride values ($P < 0.05$). No significant difference was observed between the ratio of soluble to total fluoride in national and licensed toothpastes ($P = 0.98$). In examining the uniformity of fluoride distribution, fluoride concentrations were significantly lower at the end of the tube ($P < 0.05$). The fluoride concentration values in toothpastes with NaF composition were lower but more homogeneous compared to MFP ($P < 0.05$). The absolute values of the spectrophotometric and potentiometric data differed, but they ranked similarly. In five brands, the fluoride levels measured were close to those claimed by the manufacturers.

Conclusion

Fluoride levels were evaluated ≥ 1000 ppm in 78% of toothpastes. There was no difference in fluoride levels or in the ratio of soluble to total fluoride between domestic and internationally licensed toothpastes. Toothpastes containing MFP exhibited higher fluoride concentrations than those containing NaF. Fluoride distribution was not uniform throughout the tube, and differences between total and ionized fluoride levels were observed in many brands. The spectrophotometric method can be useful as an accessible, cost-effective approach.

Introduction

Dental caries is a major public health problem worldwide, with at least 2.3 billion people suffering from permanent tooth decay and more than 530 million children suffering from primary tooth decay [1]. Given the prevalence of caries, studies have emphasized the importance of preventive approaches, especially the systemic and topical use of fluoride, with the aim of increasing the resistance of tooth enamel to acid and subsequently preventing the formation of new lesions, slowing down or even stopping the progression of existing caries, and aiding remineralization [2]. In the meantime, the frequent and topical use of fluoride toothpaste is a common approach to reducing the incidence of caries, as supported by strong scientific evidence [3, 4].

In children prone to caries, the benefits of using anti-caries toothpastes containing fluoride are considered to outweigh the risks of developing fluorosis, and, according to new recommendations, the use of fluoride toothpastes meeting the 1000–1500 ppm standard is recommended [4, 5]. In the meantime, the amount of fluoride toothpaste used should vary according to the child's age [6]. Evidence shows that reducing the fluoride concentration of toothpastes not only does not reduce the incidence of fluorosis of permanent teeth, but also reduces the effectiveness of fluoride in preventing caries [7].

Fluoride is used in toothpaste in a variety of formulations, the most common being sodium fluoride with silica abrasive; other formulations include sodium monofluorophosphate with silica abrasive or calcium carbonate. Among these formulated fluorides, only the soluble and ionized fluorides are active and can be released in saliva; due to their bioavailability, they subsequently exhibit anticaries properties, while the insoluble portion is inactive as a salt due to reaction with the abrasive. The chemical compatibility between the fluoride and abrasive components used in toothpaste affects the concentration of soluble fluoride, especially in the $Na_2FPO_3/CaCO_3$ formulation [3]; In a way that, all fluoride in the NaF/SiO_2 formulation is in the form of F^- ions and soluble, but in the $Na_2FPO_3/CaCO_3$ formulation, the soluble fluoride is in the form of ionized FPO_3^{2-}, which can be hydrolyzed over time, promoting the reaction of F^- with calcium from the abrasive and the formation of insoluble fluoride salts. Consequently, the amount of soluble and ionized fluoride is reduced [8–11].

This means that two toothpastes with the same total fluoride content can have significantly different amounts of soluble and ionized fluoride due to differences in formulation; for instance, the commonly used calcium carbonate abrasive can reduce fluoride bioavailability by 27–61% [12]. In addition to formulation, fluoride stability over time and its uniform distribution in the tube are also important factors influencing the efficacy of fluoride toothpastes [4].

Due to the insufficient fluoride content of drinking water in many regions of Iran [13], several studies have been conducted in the country to evaluate fluoride concentration and bioavailability in fluoride-containing products and to improve product quality [14–17]. Two methods are commonly used to measure fluoride: potentiometry, the gold standard, and spectrophotometry, a simpler, less expensive method [18].

Therefore, the present study aimed to determine the concentrations of total, soluble, and ionized fluoride in anti-caries paste and gel dentifrices available in the Iranian market, to investigate the uniformity of fluoride distribution in the initial and final sections of the tube, and to compare the measured values with the international standard range.

Materials and Methods

This experimental-laboratory study was conducted after obtaining the ethical code IR.MUBABOL.HRI.REC.1403.169 from Babol University of Medical Sciences, Iran. A total of 28 common brands of anticaries toothpastes (see tables in the appendix), including eight children's toothpaste brands and 20 adult toothpaste brands (21 national products and 7 products licensed by foreign companies), available in the Iranian market, were selected. The fluoride composition in seven products was sodium fluoride, and in the other products, monofluorophosphate.

Two tubes of each brand were randomly purchased from different retail centers. Whenever possible, the production dates of the two tubes differed by no more than six months, and each product had at least one year remaining before its expiration date. The toothpastes were coded, and samples were collected from the beginning and the end of each tube [3, 4].

Toothpastes with other uses, such as whitening, medicated, or herbal, were excluded from the study because their ingredients might interfere with fluoride concentration. For the study, all toothpastes were stored at room temperature under the same conditions from the time of purchase. Sampling was performed by taking two parts: the beginning (after removing 0.5 to 1 cm of the paste from the beginning of the tube) and the end of the tube (after removing 0.5 cm of the paste from the end of the tube) for each toothpaste in order to investigate the uniformity of fluoride distribution in each tube [17, 15].

Both potentiometric and spectrophotometric methods were used to measure fluoride concentrations and to evaluate the accuracy and applicability of spectrophotometry compared with the gold-standard potentiometric method.

Measurement of Fluoride Concentration of Different Toothpastes by Potentiometric Method

In the potentiometric method, fluoride concentration was measured according to the direct method described by Cury et al. using a fluoride ion-selective electrode (ELIT Ion analyser, NICO2000 Ltd, London, UK) [3, 4], and the ISO/TC 106 Dentistry SC7 Oral Care Products Working Group 4 standard was followed [12]. First, the device was calibrated with solutions with a certain concentration (0.1-5 ppm) of fluoride in order to ensure the reliability and validity of the measurement results [3, 4, 17]. In this method, the Nernst formula was used to measure fluoride concentrations [14].

The toothpastes were prepared as follows: First, a uniform suspension was prepared by mixing 110 mg of toothpaste with 10 ml of distilled water. To evaluate the total fluoride concentration, 0.25 mL of the prepared suspension was mixed with 0.25 mL of 2M HCl solution and heated in an oven (SCI FINETECH Co., Seoul, Korea) for about 1 hour at 45°C. Then, 0.5 mL of 1 M NaOH solution and 1 mL of TISAB II buffer solution (pH 5.05, prepared in the laboratory) were added. Then, the total fluoride content was measured with a fluoride ion-specific electrode [3].

To evaluate the fluoride content, the remaining suspension was centrifuged at room temperature for 10 minutes at 3000 g (PIT-Classic Premium 20000 Universal Centrifuge Pole Ideal Tajhiz Iran), and the resulting supernatant was divided into two portions for subsequent measurement of soluble fluoride and fluoride ion [3].

To measure the amount of soluble fluoride, 0.25 ml of the supernatant was added to 0.25 ml of 2 M HCl solution, which was then heated in an oven for about 1 hour at 45°C. Then 0.5 ml of 1 M NaOH solution and 1 ml of TISAB II were added, and the amount of soluble fluoride was measured by the potentiometric method [3].

Fluoride ion measurement was also possible using a 0.25 ml supernatant and 1 ml of TISAB II with 1 M NaOH and 0.25 ml of 2 M HCl solution, which could be measured with an electrode sensitive to the F^- ion [3].

Measurement of Fluoride Concentration by Spectrophotometry

In the spectrophotometric method, the Rice WE et al. method was used to evaluate the fluoride content of toothpastes, and the Lambert-Beer formula was used to measure the concentration [19, 20]. In order to read zero absorbance at any time in the absence of analyte (F^-), a control solution was first prepared to set the spectrophotometer (JASCO, UK, Ltd.); 10 ml of SPANDS solution was mixed with 7 ml of concentrated HCl solution and then made up to 100 ml by adding distilled water. To make the stock solution, 221 mg of anhydrous sodium fluoride was dissolved in 1000 ml of distilled water in a volumetric flask; then, to make the fluoride standard solution, 100 ml of the stock solution was diluted with distilled water and increased to 1000 ml [19].

To prepare the calibration curve, standard fluoride in the range of 0.1–10 ppm was prepared and 50 ml of standard solution was prepared by adding distilled water. Next, 10 ml of SPADNS-Zirconyl acid reagent solution was added to each standard solution. The spectrophotometer was adjusted to zero absorbance with the blank solution [19]. To read the absorbance, the absorbance spectrum was first evaluated, and considering the maximum absorbance of fluoride in the spectrophotometer, the absorbance readings were taken at a wavelength of 548 nm, and then the calibration curve was drawn in terms of absorbance/microgram of fluoride [19].

After performing the above steps, as of the potentiometric method, the samples were prepared by placing 1 g of dry toothpaste (to remove the interfering variable of toothpaste moisture, it was placed in an oven at 40°C for 40 minutes) in a coded polyethylene container and for digestion (conversion of fluoride

to HF), 5 ml of concentrated HCl (37%) was heated at the appropriate temperature on a hot plate in a crystallizer covered with a watch glass head for 3–4 hours with caution under the hood (due to the risk of HF escaping) until most of the HCl evaporated. Afterward, 5 ml of HCl was added again, and the solutions were transferred to a 100 mL flask. Then, 20 mL of SPADNS-Zirconyl acid reagent was added, and the volume was increased to the required amount with distilled water [19].

The absorbance of the samples was read and recorded at a visible wavelength of 548 nm. The fluoride concentration of the samples was evaluated by matching it with the calibration curve, and the amount of fluoride ion was measured [19].

All information related to each brand was recorded, and each brand and each toothpaste sample was given a code (randomly numbered from one to 28, and the second sample of the same brand was identified with a prime symbol in addition to the registered number) so that both the measurement and statistical analysis could be performed in a double-blinded and unbiased manner. In this way, the code recording and preparation for each toothpaste brand was carried out by the first project executor, and the measurement of fluoride amounts in each method was performed by an experimenter in a laboratory with equal conditions for all samples in the laboratory of the Faculty of Chemistry in Babolsar, Iran.

For statistical analysis, the data were imported into the SPSS (version 27) software (IBM, USA) after collection and analyzed using descriptive statistics and inferential tests, including the paired t-test. In cases where the data were not normally distributed, nonparametric tests were used for analysis. In addition, a P value < 0.05 was considered statistically significant.

Results

Among the 28 fluoride toothpaste brands evaluated, five did not report the fluoride concentration on the tube packaging. Among the remaining products, only three brands showed total fluoride concentrations that were relatively consistent with the labeled fluoride concentrations declared by the manufacturers, with differences of 4.7%, 9.2%, and 11%, respectively. Similarly, the soluble fluoride concentrations of two toothpaste brands were close to the manufacturers declared values, differing by only 1% and 14%, respectively (Table 1).

In the evaluation of toothpastes intended for both adults and children, the total fluoride concentrations of toothpaste codes 3, 9, 10, 24, and 26 were within the recommended standard range. In addition, the soluble fluoride concentrations of toothpaste codes 2, 4, 8, 12, 14, and 21 were also within the standard range (Table 1). Overall, toothpaste codes 16, 17, 18, 20, 25, and 27 contained less than 1000 ppm fluoride, whereas 78% of the evaluated toothpastes contained fluoride concentrations exceeding 1000 ppm.

Regarding the comparison of the ratio of soluble fluoride to total fluoride in national and foreign-branded toothpastes (see tables in the appendix), independent t-test and Levene's test were used, which indicated that there was no statistically significant difference between the two groups (P = 0.98).

Table 1
Comparative study of fluoride levels of common toothpastes on the market.

Comparison of Fluoride Levels		Code 1	Code 2	Code 3	Code 4	Code 5	Code 6	Code 7	Code 8	Code 9	Code 10
Total Fluoride	Average	3109.405	2769.65	1152.788	2676.795	2577.648	2549.928	3749.418	2430.343	1530.32	1332.862
	SD	731.104	1165.46	148.913	241.072	979.322	828.184	1163.906	2292.034	1218.705	240.418
Soluble Fluoride	Average	1846.425	1146.275	401.872	1306.868	818.881	858.54	3436.795	1465.773	1688.958	864.71
	SD	724.768	582.804	282.875	637.322	193.237	228.999	1802.953	1588.983	125.617	657.879
Ionized Fluoride	Average	622.0	696.67	288.877	601.565	489.46	589.002	553.207	447.38	5476.615	459.717
	SD	215.524	208.0571	140.010	166.866	148.969	207.866	402.057	385.451	9565.154	282.694
P		0.010	0.019	0.023	0.015	0.012	0.015	0.024	0.199	0.368	0.077

Comparison of Fluoride Levels		Code 11	Code 12	Code 13	Code 14	Code 15	Code 16	Code 17	Code 18	Code 19	Code 20
Total Fluoride	Average	2235.687	3567.712	3313.975	2024.64	3169.297	736.812	552.397	983.577	3653.505	767
	SD	1045.643	1440.400	1444.773	781.581	1179.068	561.793	151.097	304.076	1374.769	438.459
Soluble Fluoride	Average	2106.795	1587.785	2027.477	1122.925	1754.72	660.025	273.567	775.107	1797.21	563.292
	SD	552.905	763.033	500.037	493.187	272.931	183.118	62.389	341.670	671.916	140.974
Ionized Fluoride	Average	640.415	508.892	691.405	482.907	851.055	299.707	6875.145	249.302	1699.48	249.345
	SD	828.164	313.345	511.118	206.399	433.232	356.512	37.473	176.889	699.376	232.882
P		0.102	0.013	0.017	0.014	0.010	0.174	0.010	0.031	0.059	0.092

Comparison of Fluoride Levels in Children Toothpastes		Code 21	Code 22	Code 23	Code 24	Code 25	Code 26	Code 27	Code 28
Total Fluoride	Average	2539.202	1656.180	4246.167	1330.002	841.162	1243.815	761.215	3088.160
	SD	1047.541	1230.415	2447.563	589.764	635.464	423.690	232.141	1331.424
Soluble Fluoride	Average	1571.597	862.789	1634.121	844.782	220.382	571.012	443.942	1647.880
	SD	212.647	285.405	512.661	143.472	87.085	244.382	179.810	1918.371
Ionized Fluoride	Average	603.185	338.925	564.537	28253	184.617	397.807	317.072	368.062
	SD	267.750	89.233	296.355	166.607	155.619	241.299	122.954	209.424
P		0.018	0.018	0.008	0.015	0.024	0.024	0.043	0.029

Concentration of different fluoride levels in each toothpaste is in ppm.

To compare soluble and ionized fluoride with total fluoride, the Kruskal-Wallis test was used.

To compare soluble and ionized fluoride with total fluoride, the nonparametric Kruskal-Wallis test was used. If the results of the test (Table 1) indicated a significant difference, a supplementary paired comparison test with Bonferroni adjustment was used to more accurately identify the differences. There was no significant difference between the total and soluble fluoride values in all toothpastes. However, there was no significant difference in the comparison of ionized fluoride values with total fluoride in toothpastes with codes 8, 9, 10, 11, 16, 19, and 20 ($P > 0.05$); nevertheless, this difference was observed in the rest of the toothpastes ($P < 0.05$) (see tables in the appendix).

Furthermore, according to the paired t-test (Table 2), in 93% of the cases, total fluoride was higher at the beginning of the tube than at the end of the tube; this difference was more pronounced in the case of code 8. In the case of soluble fluoride, 75% had less soluble fluoride at the end of the tube, with the most pronounced difference observed in code 2. However, in the case of ionized fluoride distribution, 54% had more ionized fluoride at the end, with the most pronounced difference in code 9, and in 46% of the cases, the amount of ionized fluoride was lower at the end of the tube, with the most pronounced difference in code 11.

Table 2
Comparison of fluoride levels in ppm at the beginning and end of each tube of toothpaste.

Comparison		Code 1	Code 2	Code 3	Code 4	Code 5	Code 6	Code 7	Code 8	Code 9	Code 10
Beginning-Total	Average	3593.20	3296.17	1212.28	2787.07	3380.34	3048.5	4421.6	4383.15	2386.84	1340.36
	SD	379.44	1720.94	222.35	337.09	499.62	290.16	1402.16	699.94	1225.89	164.6
End-Total	Average	2625.60	2241.96	1093.29	2566.52	1774.95	2051.35	3077.23	477.53	673.8	1325.36
	SD	723.40	43.50	54.086	109.88	288.45	539.11	539.11	821128.5	135.2	382.1
Beginning- Soluble	Average	2000.85	1639.38	349.28	1784.67	741.38	1055.01	4856.63	2680.64	1608.22	1417.32
	SD	1212.03	49.78	48.24	238.08	288.45	30.32	1169.23	1291.13	93.35	277.28
End-Soluble	Average	1691.99	653.16	454.46	829.06	896.37	662.06	2016.95	250.90	1769.69	312.1
	SD	107.02	209.46	476.09	498.67	69.25	44.63	566.58	95362.72	111.60	4.64
Beginning-Ionized	Average	736.93	525.69	327.98	480.36	617.95	617.95	619.98	619.98	924.3	225.47
	SD	136.7	29.18	210.09	157.38	20.34	20.03	420.07	21.35	10028.4	693.96
End-Ionized	Average	507.07	867.65	249.77	722.77	360.96	560.05	486.43	541.65	13817.9	109.33
	SD	260.39	109.88	92.48	0.0	11.419	354.78	539.11	640.95	2898.63	885.76

Comparison		Code 11	Code 12	Code 13	Code 14	Code 15	Code 16	Code 17	Code 18	Code 19	Code 20
Beginning-Total	Average	3112.03	4637.29	4191.33	2672.21	3968.75	1208.85	605.41	1185.96	4721.87	1026.78
	SD	275.84	1097.12	1727.80	72.11	1250.49	227.20	73.25	335.41	977.51	409.54
End-Total	Average	1359.34	2498.13	2436.61	1377.06	2369.84	264.77	499.38	781.19	2585.13	507.22
	SD	363.42	666.74	444.69	387.28	224.35	62.59	227.78	36.05	385.73	373.37
Beginning- Soluble	Average	2434.99	2072.39	2117.72	1464.65	1916.59	792.64	302.3	932.64	2355.27	670.12
	SD	681.62	196.29	135.63	511.04	48.07	173.10	9.72	408.15	329.65	78.95
End-Soluble	Average	1778.59	1103.17	1937.23	781.19	1592.84	527.40	244.83	617.57	1239.15	456.46
	SD	147.08	876.77	836.14	36.05	341.21	16.69	90.99	290.44	4.58	87.97
Beginning-Ionized	Average	1054.61	702.53	889.5	582.89	980.96	482.55	128.69	373.13	2219.70	326.50
	SD	1170.95	335.37	740.56	47.74	674.18	490.45	25.18	169.77	524.80	342.88
End-Ionized	Average	226.22	315.25	493.31	382.92	721.15	116.86	162.68	125.47	1179.25	172.18
	SD	14.31	179.38	279.87	292.46	202.6	83.80	49.22	60.93	330.79	146.01

Comparison		Code 21	Code 22	Code 23	Code 24	Code 25	Code 26	Code 27	Code 28
Beginning-Total	Average	3356.46	2299.43	5784.18	1696.85	1145.94	1604.17	704.15	3452.78
	SD	384.831	1696.33	2831.22	683.91	909.79	122.47	341.10	2015.68
End-Total	Average	1721.94	1012.93	2708.15	963.15	536.38	885.45	818.27	2723.53
	SD	687.22	95.55	702.8	193.44	110.13	83.81	179.19	850.45
Beginning- Soluble	Average	1753.50	1101.149	2046.9	900.83	216.15	708.60	582.75	2691.97
	SD	20.34	116.35	232.29	11.99	120.76	18.88	20.09	2584.56
End-Soluble	Average	1389.69	624.43	1221.34	788.73	224.75	433.42	305.13	603.79
	SD	53.68	60.93	230.5	221.06	89.7	321.91	139.52	0
Beginning-Ionized	Average	735.72	373.93	812.61	468.22	161.6	537.83	418.85	316.87
	SD	236.34	129.97	128.19	110.15	20.38	301.33	15.35	174.38
End-Ionized	Average	470.65	303.92	316.46	202.34	207.63	257.78	215.29	419.25
	SD	300.81	47.43	29.12	19.58	193.9	72.51	60.69	301.57

The next comparison in this study is regarding the soluble and ionized fluoride of different fluoride salts in toothpastes (Table 3). In the Iranian market, fluoride is used in toothpastes in two forms: monofluorophosphate (MFP) and sodium fluoride (NaF). In this study, only seven brands contained NaF, while the rest used MFP. The independent t-test was used for comparison. According to the results, the fluoride content in toothpastes containing NaF was significantly lower than that in MFP toothpastes, but it was more homogeneous. Moreover, in both fluoride-containing compounds, the amounts of ionized fluoride were lower, and the data had less dispersion.

Table 3
Comparison of soluble and ionized fluoride levels in ppm of different toothpastes by the type of fluoride salt.

Fluoride-containing Compound		Average	SD	Standard Error	Significance Level*
Soluble	MFP	1492.281	957.0821	107.005	⍰0.001
	NaF	691.370	413.455	78.135	⍰0.001
Ionized	MFP	593.863	431.698	48.265	⍰0.001
	NaF	283.314	197.549	37.333	⍰0.001
*Independent T-Test					

To compare the newer spectrophotometric method with the potentiometric method (Table 4), the initial fluoride values of toothpastes were determined using both methods. Despite the difference in absolute values, the relative rankings of some brands were almost the same in both methods, such that in both methods, codes 12, 13, 19, and 23 were in the high ranks in terms of fluoride concentration, and 18, 17, 16, and 27 were among the brands with the lowest fluoride concentration in both methods. This correlation indicates that although the numbers reported by the two methods differ, both methods can distinguish "strong" and "weak" brands in terms of fluoride content to some extent. The spectrophotometric data also indicated less dispersion compared to potentiometric data.

Table 4
Comparison of fluoride levels in ppm evaluated in spectrophotometric and potentiometric methods

Comparison of Two Methods		Code 1	Code 2	Code 3	Code 4	Code 5	Code 6	Code 7	Code 8	Code 9	Code 10
Potentiometry	Average	3593.20	3296.17	1212.28	2787.07	3380.34	3048.5	4421.6	4383.15	2386.84	1340.36
	SD	379.44	1720.94	222.35	337.09	499.62	290.16	1402.16	699.94	1225.89	164.43
Spectrophotometry	Average	3537.8	3510.18	2844.67	3257.34	3537.85	3422.87	3362.00	3469.7	2533.68	2431.67
	SD	69.03	50.46	34.46	80.01	69.03	83.52	47.66	192.16	416.32	611.52

Comparison of Two Methods		Code 11	Code 12	Code 13	Code 14	Code 15	Code 16	Code 17	Code 18	Code 19	Code
Potentiometry	Average	3112.035	4637.295	4191.335	2672.215	3968.755	1208.855	605.41	1185.96	4721.875	1026
	SD	275.8494	1097.126	1727.808	72.11782	1250.497	227.2005	73.25626	335.413	977.5115	409.7
Spectrophotometry	Average	3384.47	3216.48	3456.911	3192.507	3465.749	2933.72	2646.188	2845.833	3555.453	2709
	SD	35.2803	37.96476	35.8621	146.252	78.96671	443.7789	204.192	108.5208	151.8591	278.3

Comparison of Two Methods in Children Toothpastes		Code 21	Code 22	Code 23	Code 24	Code 25	Code 26	Code 27	Code 28
Potentiometry	Average	3356.465	2299.43	5784.18	1696.85	1145.945	1604.175	704.155	3452.79
	SD	384.5883	1696.335	2831.227	683.9137	909.7989	122.478	341.1012	2015.69
Spectrophotometry	Average	3362.128	2573.004	3475.992	2602.409	2654.778	3072.654	2494.946	3085.54
	SD	107.0022	114.2447	189.4734	307.9234	28.73641	18.57353	268.3233	104.315

Discussion

Based on the measured total and soluble fluoride concentrations, 71% of the toothpastes were within the standard range of 1000–1500 ppm [4, 5]. According to the FDI statement [21], which recommends over-the-counter toothpastes with standard fluoride concentrations and a minimum bioavailable fluoride level of 800 ppm, 82% of the products were considered favorable in terms of fluoride bioavailability.

In 10% of the toothpastes, both total and soluble fluoride concentrations exceeded 1500 ppm. Therefore, the exact fluoride concentration should be clearly stated on the packaging to ensure appropriate use. However, the results of the present study showed that in most cases where total fluoride exceeded the standard range, the soluble fluoride concentration was lower and closer to 1500 ppm. This finding may indicate the presence of some fluoride in an insoluble form or combined with formulation components, which may not be directly biologically available. The results of a study by Movahed et al. [17] were consistent with the present study and high-fluoride toothpastes (> 1500 ppm F) may represent a practical alternative where prescription-strength toothpastes containing 5000 ppm fluoride are unavailable or difficult to access for high-caries-risk populations.

According to the minimum fluoride concentration required to provide anti-caries properties (1000 ppm), in the present study, 22% of the toothpastes were evaluated to have fluoride levels below the minimum required, as the majority of the toothpastes were within the standard range, which is consistent with other international studies [4, 8, 9]. However, this finding is inconsistent with the results of a study on toothpastes available on the Argentine market, which found that 67% of the products lacked sufficient fluoride for anticaries effects [3]. Several lines of evidence indicate that toothpastes containing less than 1000 ppm fluoride are less effective at preventing caries, especially dentinal caries, than standard products [7]. Therefore, considering the low fluoride levels in drinking water in Iran [13] and the high prevalence of caries in children and adults [22, 23], fluoride toothpaste is of particular importance for preventing caries, especially on smooth surfaces, and the use of these toothpastes is not recommended for daily use [4, 5]. In our study, among these toothpastes with fluoride levels below the minimum standard, 33% and 52% were for children and adults, respectively, and there are different standards regarding the fluoride content of children's toothpastes [24]. However, in the case of adult toothpastes, the total fluoride content must be within the standard range and at least 1000 ppm. Among these toothpastes, only one had much less total fluoride than the company claimed, and in the rest, the company's claim was less than 1000 ppm or was not recorded.

A wide range of total, soluble, and ionized fluoride concentrations was observed among the evaluated products, indicating substantial heterogeneity in fluoride formulation and availability across commercially available toothpastes. It noteworthy that at all fluoride concentration levels, the data variation was high. Nevertheless, for ionized fluoride, the values were closer, except for one, which was even higher than the total fluoride in the toothpaste itself and the maximum total fluoride among all toothpastes. This distinctive behavior may be related to formulation-specific factors, including differences in fluoride release characteristics and chemical equilibrium within the toothpaste matrix according to Le Chatelier's principle, especially in conditions where fluoride is present in the product as poorly soluble compound [25].

Regarding the comparison of different fluoride concentrations, no difference was observed between total and soluble fluoride levels, as well as soluble and ionized fluoride levels, in all toothpastes. However, there was a difference between total and ionized fluoride in 75% of the toothpastes. This finding is consistent with the study conducted by Pérez et al. [9], which reported no difference between total and soluble fluoride.

In total, 17% of the fluoridated toothpastes did not have fluoride content listed on the tube, and in only 17% of the products, the measured fluoride content was close to the company's claim. The results of the present study are consistent with previous national studies [15, 17] and some international investigations [8, 9, 26].

In this study, monofluorophosphate was the predominant fluoride compound (75%), and silica was the main abrasive used (82%). The use of silica is considered an advantage, especially in monofluorophosphate-containing formulations, due to its better chemical compatibility [8–11]. Toothpastes containing monofluorophosphate showed higher levels of total, soluble, and free-ion fluoride than those containing sodium fluoride, although studies have shown that the stability and bioavailability of fluoride in monofluorophosphate formulations may decrease over time and under storage conditions [4, 11, 12], leading manufacturers to use higher initial fluoride levels.

Moreover, in the present study, all toothpastes contained a single fluoride compound, except for one brand, which contained both fluoride compounds. However, in Pérez et al. [9], 10% of toothpastes contained both MFP and NaF salts. The possible reason for using the combination of these two compounds is to create a synergistic effect, such that sodium fluoride acts as a fast-acting source and monofluorophosphate as a slow-release source of fluoride, thereby increasing the duration of the protective effect of fluoride [27]. Regarding the optimal fluoride dose, it has also been recommended in preventive dentistry to minimize rinsing or to remove it to maximize the effectiveness of fluoride toothpaste [28].

One of the important findings of this study was a significant difference in total and soluble fluoride concentrations between the beginning and end of the toothpaste tube, with higher values observed at the beginning, which, together with the high standard deviation, indicates a non-uniform distribution of fluoride in the products; a phenomenon that has also been reported in previous national studies [15, 17], In contrast, Movahed et al. [17] reported higher fluoride concentrations at the end of the toothpaste tubes. This finding indicates that the uniformity of fluoride distribution remains a challenge in the production of toothpastes available in the Iranian market.

Furthermore, according to this study, there was no difference in fluoride availability characteristics or the soluble-to-total fluoride ratio between national toothpastes and those under the franchise of foreign companies, which is consistent with Pakdaman's study [14]. However, in Pakdaman's study, domestic toothpastes were compared with imported ones.

Finally, a comparison of the spectrophotometric method with the potentiometric method indicated that, despite the difference in absolute values, the relative rankings of the brands in the two methods were similar. Its acceptable sensitivity, good reproducibility, and lower cost make the spectrophotometric method a practical alternative for large-scale screening studies [29].

Strengths and Limitations

The main strengths of the present study include the simultaneous assessment of total, soluble, and ionized fluoride, which enables a more accurate assessment of fluoride bioavailability and the anticaries potential of toothpastes. Moreover, the comparison of spectrophotometry and potentiometry methods shows the applicability of less expensive analytical methods for studies with large sample sizes. The study of fluoride distribution at the beginning and end of the tube and the appropriate diversity of children and adult brands, both national and internationally licensed toothpastes, are other strengths of this study, which increase the generalizability of the results to the Iranian market.

In contrast, the present study involved some limitations. The measurements were performed over a fixed time period, and changes in fluoride concentration during storage were not examined, while fluoride stability, especially in monofluorophosphate formulations, may be affected by storage conditions. In addition, direct assessment of fluoride bioavailability under clinical conditions or in simulated oral environments was not performed, and other formulation factors, such as pH and abrasive type, were not separately examined.

Conclusion

The findings of the present study showed that most of the evaluated toothpastes contained fluoride concentrations at or above the minimum level recommended for caries prevention. However, considerable variability was observed in fluoride concentration, bioavailability, and distribution within toothpaste tubes. In addition, discrepancies between the measured fluoride content and manufacturers' claims, as well as the absence of fluoride labeling in some products, highlight the need for stricter quality control and more accurate product labeling. No significant differences were observed between domestic and foreign-licensed toothpastes regarding fluoride availability. Furthermore, the spectrophotometric method demonstrated potential as a practical and cost-effective alternative for fluoride analysis in large-scale studies and screening programs.

Declarations

Ethics approval and consent to participate:

This experimental laboratory study was approved by the Ethics Committee of Babol University of Medical Sciences, Iran (Approval No. IR.MUBABOL.HRI.REC.1403.169). As the study did not involve human participants or animals, informed consent was not required.

Consent for publication:

Not applicable

Competing interests:

The authors declare that they have no competing interests

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Author Contribution

Z.Y. and M.G. conceived and designed the study. Z.Y. performed the laboratory experiments and collected the data. M.J.C. provided technical expertise on the analytical methods (spectrophotometry and potentiometry) and supervised the chemical analyses. Z.Y. and M.G. performed the statistical analysis and drafted the initial manuscript. M.G. and M.J.C. critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Data Availability

The datasets generated and analyzed during the current study are not publicly available due to data protection policies but are available from the corresponding author on reasonable request.

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