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Total and free available fluoride in toothpastes in Brunei, Cambodia, Laos, the Netherlands and Suriname

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Objectives: This study assessed total and free fluoride concentrations in samples of toothpaste from Brunei, Cambodia, Laos, the Netherlands and Suriname, and investigated the labelling practices of the respective manufacturers. **Materials and methods:** Convenience samples were bought in the five countries and sent for analysis to the Netherlands. Levels of total and free available fluoride were measured. Details of the information declared on the packaging about type of fluoride and abrasives were recorded, and manufacturing and expiry dates were noted. **Results:** A total of 119 samples of toothpaste were analysed. With one exception, all samples from the Netherlands complied with ISO (International Organisation for Standardisation) labelling requirements and there were no differences between the fluoride content declared and that found to be present on analysis. In samples purchased in the other countries, sodium monofluorophosphate (SMFP) toothpastes predominantly showed a low percentage of free available fluoride and the majority of toothpastes did not follow standard labelling guidelines. **Discussion:** This study is not representative of any of the brands analysed, yet it highlights problematic discrepancies in products across countries. These may be related to the lack of a generally accepted methodology for analysing total and free fluoride content, absence of an agreement on the minimum concentration of fluoride required to ensure efficacy, weak regulating institutions that are unable to control labelling and consumer information, as well as a possible influx of counterfeit low-quality toothpaste. **Conclusions:** Renewed international focus should be directed towards closing gaps in guidelines and standards. Consumers should use only non-expired toothpaste, which should preferably be silica-based fluoride toothpaste that does not include abrasives containing calcium and that is properly labelled.

Key words: *Fluoride toothpaste, free available fluoride*

The global epidemic of dental decay affects > 90% of the world's population; 40–90% of 12-year-olds suffer from dental decay and its consequences, such as pain, chronic infection, absenteeism from school, and physical and learning problems, as well as low quality of life. In low-income countries, almost all dental decay remains untreated[1,2].

A group of experts convened in Geneva for the *Global Consultation on Oral Health through Fluoride* (2006) stated that 'prevention by using fluoride is the only realistic way of reducing this [caries] burden in populations'[3]. A subsequent call to action emanating from a joint meeting of the World Health Organisation (WHO), FDI World Dental Federation and International Association for Dental Research (IADR) in Beijing in 2007 stated that:

- 'Fluoride toothpaste remains the most widespread and significant form of fluoride used globally and the most rigorously evaluated vehicle for fluoride use'[4]
- 'The effectiveness of fluoride toothpaste has been assessed since the 1940s in over 100 clinical trials and the anti-tooth decay (anti-caries) efficacy of fluoride toothpaste has been confirmed'[4]
- 'Fluoride toothpaste is safe to use irrespective of low, normal or high fluoride exposure from other sources'[4].

This call to action strongly recommends the promotion of effective fluoride toothpaste for the mass prevention of tooth decay. In this context, the issue of the effectiveness of fluoride toothpaste is of paramount importance.

Some of the earliest fluoride toothpastes tested in clinical trials in the 1940s and 1950s were not effective against caries[5–7]. These findings, which were not understood at the time, were later explained as resulting from the formation of insoluble calcium fluoride (CaF_2) caused by the reaction of free F^- with chalk-based abrasives[8]. For fluoride toothpaste to be effective, it

must contain an appropriate concentration of free available fluoride. This implies that added fluoride is not chemically bound to other ingredients in the toothpaste. In toothpastes with NaF, NH_4F and SnF_2, the fluoride compounds are not compatible with abrasives that contain calcium [e.g. calcium carbonate ($CaCO_3$), dicalciumphosphate (dehydrate) (DCPH), calcium glycerophosphate (CGP), tricalciumphosphate (TCP)]. By contrast, in sodium monofluorophosphate toothpaste [SMFP (Na_2PO_3F)], the PO_3F^{2-} component has greater compatibility with calcium-containing abrasives. This is because in PO_3F^{2-} the fluoride is firmly bound to the phosphate and therefore cannot bind to soluble calcium to form insoluble calcium fluoride[9].

In the oral cavity, the protective action in SMFP toothpastes results either from the direct effect of the PO_3F^{2-} group or from the release of fluoride by hydrolysis in the oral cavity[10,11].

A previous study of toothpastes purchased in low-income countries found that in 25% of the toothpastes, < 55% of the declared fluoride was in free available form[12]. A study in Brazil reported that 13 out of 14 SMFP toothpastes with calcium-containing abrasives used by children contained 15–50% less free available fluoride than the total fluoride content. By contrast, in all the NaF toothpastes with silica abrasive, almost all the fluoride was available in free (ionised) form[13]. These findings raise questions about the compatibility of a PO_3F^{2-} component with calcium-containing abrasives.

Another important issue relevant to the quality of fluoride toothpaste concerns the provision of consumer information through correct labelling. Standards in this context are defined by the International Organisation for Standardisation (ISO) in its standard ISO 11609 (2010). However, huge variations in compliance with ISO labelling requirements are seen in different brands of fluoride toothpaste[12].

The present study aimed to assess labelling practices, as well as the amount of total and free available fluoride in samples of fluoride toothpastes purchased in Brunei, Cambodia, Laos, the Netherlands and Suriname. Results are discussed and recommendations for improving toothpaste quality are made.

MATERIALS AND METHODS

Fluoride toothpaste samples

Samples of fluoride toothpastes were purchased in countries in which the present authors had reliable contacts who were able to collaborate and forward samples for analysis. Samples collected in the Netherlands included toothpastes intended for use by young children (< 5 years of age) (n = 27) and adults (n = 19); all were registered by the Keuringsdienst van Waren (Dutch Food and Drug Administration).

Fluoride toothpastes from Suriname (n = 18) were purchased in shops in the capital Paramaribo. Fluoride toothpastes from Brunei (n = 20) were purchased from a supermarket in the capital city Bandar Seri Begawan. In Cambodia and Laos fluoride toothpaste samples (n = 14 and n = 21, respectively) were purchased in the central market of the capital Phnom Penh, and in small shops in Vientiane, respectively.

Information provided on packaging

All toothpaste samples were checked for information provided on the packaging (either the outer carton or the tube itself). The country of production was recorded if available. The information on the package was checked for descriptive names of the fluoride component and its concentration in parts per million (ppm). If only the percentage w/w of NaF, SnF_2 or Na_2PO_3F was declared, the parts per million F (ppm F) were calculated. Descriptive names of abrasives on the packaging were recorded. In toothpastes in which both silica and calcium-containing abrasives were declared, the calcium-containing abrasive was recorded. In two cases in which the date of production was declared on the package, the expiry date was recorded as three years later. If the expiry date was indicated, it was recorded. All tests for fluoride content were performed in the Netherlands within six months after purchase.

Total fluoride measurements

Closed toothpaste tubes were carefully squeezed in order to mix the contents. The tubes were then opened and the first few grams of toothpaste to emerge from the tube were discarded. Two separate portions of 50 mg each were then squeezed from the tube for duplicate fluoride content measurements. Each of these two portions was diluted in 2 mL 1 M HCl and mixed thoroughly until no toothpaste visibly adhered to the vessel. The samples were mounted in an overhead rotator for one hour at 4 °C, after which 2 mL of toluene reagent was added. After overnight overhead rotation at 4 °C, samples of the toluene reagent phase were injected into a gas chromatograph (Gas Chromatograph CP9001; Chrompack International BV, Middelburg, the Netherlands) with a wide-bore injection system and two bore columns of 10 m and 25 m (WCOT fused silica with a coating of CP-SIL-5 CB). The toluene reagent was freshly made by mixing 90 mL toluene (Sigma-Aldrich GmbH, Steinheim, Germany) with 1 mL trimethylchlorosilane (Chrompack International BV) and 10 mL isopentane (Merck BV, Schiphol-Rijk, the Netherlands) stock solution of 0.1% isopentane in toluene[12].

Measurements of free available fluoride

Approximately 4 g of the duplicate toothpaste samples were suspended in water at a 1:3 dilution and shaken with a stainless steel ball by hand for two minutes. Then the slurries were centrifuged (Eppendorf AG, Hamburg, Germany) for two minutes at 16,110 ***g*** and the supernatants collected. The supernatants were diluted at 1:20 with Milli Q water and treated with four units of acidic phosphatase (Sigma Chemical Co., St Louis, MO, USA) for each 12.5 mg of toothpaste. Acidic phosphatase was dissolved in a fresh mixture with final concentrations of 89 mM NaAc (Merck BV) and 116 mM glacial acetic acid (Merck BV) adjusted to pH 4.8 with potassium hydroxide (KOH). After digestion at room temperature for 24 hours, fluoride was measured with the fluoride electrode. Samples of the phosphatase supernatant mixtures were diluted with Tisab buffer [0.3 M potassium hydrogen phthalate ($C_8H_5KO_4$), 0.21 M KOH, 1 M KNO_3 (all chemicals from Merck BV)]. The fluoride ion was measured with a fluoride electrode (F1052F; Radiometer AS, Copenhagen, Denmark) connected to a digital pH meter (PHM 63; Radiometer AS). This method was used to measure all soluble fluoride; resulting fluoride measurements are referred to as measurements of free available fluoride.

RESULTS

The duplicate analysis of separately prepared samples and subsequent fluoride measurement revealed a duplicate measurement error [$\sqrt{\sum(x_1 - x_2)^2/2n}$] for the total fluoride measurement of 29 ppm F and for the free available fluoride measurement of 61 ppm F.

Most of the toothpastes for children aged < 5 years and adults in the Netherlands were NaF toothpastes, but seven toothpastes contained Na_2PO_3F and two contained Na_2PO_3F in combination with NaF. Four toothpastes contained NH_4F. One toothpaste for children aged < 5 years declared a fluoride content of 260 ppm F but showed 239 ppm F in the test. Two toothpastes for young children that declared fluoride content of 400 ppm F were found to contain 356–374 ppm F in the test. All toothpastes for young children that declared fluoride content of 500 ppm F were found to show fluoride contents of 442–554 ppm F in the tests. All fluoride toothpastes for young children in the Netherlands (n = 27) contained > 70% free available fluoride except one brand (*Table 1*). The manufacturer of this brand adjusted the composition of the toothpaste after being informed that the free available fluoride was low. One adult toothpaste did not declare its fluoride content, which was shown on testing to be 760 ppm F. The five

Table 1 Results of analyses of fluoride toothpastes for children aged < 5 years purchased in the Netherlands in January 2006 and analysed in February 2006

Lab no.	Label	F compound on label	ppm F calculated	Total ppm F in analysis	% free F of total in analysis
1	Edah Duck Toddler	NaF	260	239	77
2	Colgate My First 0–6	NaF	400	356	100
3	Colgate My First 0–6	NaF	400	374	100
4*	Kruidvat Toddler	NaF	500	442	41
5	Trekpleister Kids 44240742	NaF, Na_2PO_3F	500	489	90
6	Trekpleister Kids 44396343	NaF, Na_2PO_3F	500	454	100
7	Trekpleister Toddler 44398788	NaF	500	458	100
8	TheraMed Junior	NaF	500	449	89
9	DA Toddler toothpaste	NaF	500	492	97
10	DA Toddler 44240416	NaF	500	493	94
11	DA Toddler 44398494	NaF	500	472	99
12	Zendium Toddler	NaF	500	482	79
13	Zendium Toddler Mice	NaF	500	468	73
14	Elmex Toddler	NH_4F	500	456	96
15	Prodent Toddler Tinky Winky	NaF	500	489	80
16	Sensodyne Sesamstr Junior 0–5	Na_2PO_3F	500	537	100
17	EtosToddler 44221845	NaF	500	459	86
18	Etos Toddler 44397986	NaF	500	457	95
19	Edah Mildfris for Kids	NaF	500	452	94
20	Schlecker AS-dent	NH_4F	500	480	76
21	Schlecker AS-dent Framboos	NaF	500	554	71
22	AS-dent Softmint	NH_4F	500	537	72
23	AS-dent Framboos	NaF	500	474	84
24	HEMA Jip & Janneke	NaF	500	454	100
25	HEMA Everclean Child 0–4	NaF	500	480	81
26	Oral B Stages	NaF	500	462	100
27	Periodent Zahngel fur Kinder	Na_2PO_3F	500	506	100

*Later adjusted by the producer and not included in the calculation of the mean.

toothpastes declaring content of 1000 ppm F were found to contain 936–1082 ppm F, and the 11 toothpastes declaring content of 1100 ppm F were found to contain 1005–1078 ppm F. One toothpaste claiming 1350 ppm F contained 1303 ppm F, and one toothpaste stating 1400 ppm F contained 1306 ppm F. All adult fluoride toothpastes (n = 19) contained > 90% free available fluoride (*Table 2*). The mean concentration of free available fluoride in all toothpastes obtained in the Netherlands was 94%.

Information on and test results for toothpastes from Brunei, Cambodia, Laos and Suriname are presented in *Tables 3–6*. In total, 73 toothpastes were tested, including five toothpastes for young children from Laos with a declared fluoride content of 500 ppm F (a calculated 498–501 ppm F). In two cases the country of manufacture could not be retrieved from the information on the package. The expiry or production date could only be retrieved from 21 of the 73 toothpastes. Six of these toothpastes had an expiry date that was < 1 year from the date of purchase. The packaging of 13 of the 73 toothpastes contained no information on the abrasive. Seventeen toothpastes did not declare the fluoride concentration. Three of the toothpastes declared to be fluoride toothpastes did not contain any fluoride and another three contained < 300 ppm F. The remaining 67 toothpastes, except the five toothpastes for children aged < 5 years from Laos, contained 899–1659 ppm F according to the tests. Of the remaining 67 toothpastes including the five toothpastes for young children, 37 contained Na_2PO_3F and 30 contained only NaF. Of the 37 toothpastes containing Na_2PO_3F, 17 had < 50% free available fluoride (*Table 7*). With one exception these 17 Na_2PO_3F toothpastes contained calcium-based abrasives according to the information on the package. The mean concentration of free available fluoride in Na_2PO_3F toothpastes with a calcium-containing abrasive was 53.2%, which was statistically significantly lower than the mean free available fluoride concentration of 90.4% in NaF toothpastes with silica (Student's t-test, $P < 0.001$) (*Table 7*). The mean concentration of free available fluoride in NaF toothpastes that did not declare an abrasive was 95.7%. All 30 NaF toothpastes contained > 70% free available fluoride and only eight contained 70–80% free available fluoride.

DISCUSSION

Limitations of the study

The study has several limitations and therefore its results should be interpreted with caution. These limitations include:

- Sampling: the toothpaste samples included in the study were not obtained in a systematic manner. Because of the small sample size and the geographical focus of the five countries selected, the results cannot be considered representative of fluoride content or labelling quality of any particular brand. Labelling in particular can show large variations from country to country. Although we list the respective brand names in the result tables, we do not imply that other samples of these brands, or the brand overall, would show the same results in further analysis
- Analysis methodology: currently, there is no standardised methodology to measure free available fluoride concentrations in toothpaste. The description of a testing method, originally included in ISO Standard 11609, was taken out of the standard and is subject

Table 2 Results of analyses of adult fluoride toothpastes purchased in the Netherlands in January 2006 and analysed in February 2006

Lab no.	Label	F compound on label	ppm F calculated	Total ppm F in analysis	% free F of total in analysis
28	Snoopy	Na_2PO_3F	?	760	100
29	DA Junior 44240432	Na_2PO_3F	1000	993	100
30	DA Junior 44398516	Na_2PO_3F	1000	978	100
31	Oral B Stages	NaF	1000	1082	100
32	Kauboy Happy Minze	NaF	1000	972	100
33	Kauboy Happy Frucht	NaF	1000	936	100
34	Colgate Bugs Bunny 44240297	NaF	1100	1036	100
35	Colgate Bugs Bunny 44399458	NaF	1100	1022	100
36	Colgate Tweety	NaF	1100	1039	100
37	HEMA Jip & Janneke 5–12	NaF	1100	1022	97
38	HEMA Space Boyz 5–12	NaF	1100	1007	100
39	HEMA Shiny Girlz 5–12	NaF	1100	1015	100
40	Kruidvat Ultradent Junior	NaF	1100	1005	100
41	Oral B Stages Fruit power rangers	NaF	1100	1078	94
42	Prodent Rocket Power 44396025	NaF	1100	1027	98
43	Prodent Rocket Power 44399687	NaF	1100	1015	100
44	Prodent Rocket Power 44399695	NaF	1100	1032	100
45	Aquafresh Junior mild & minty	NaF	1350	1303	92
46	Elmex Junior 5–12	NH_4F	1400	1306	100

Table 3 Results of analyses of fluoride toothpastes purchased in Brunei in November 2007 and analysed in March 2008

Lab no.	Label	Country of manufacture	Expiry date	Abrasives	F compound on label	ppm F calculated	Total ppm F in analysis	% free F of total in analysis
301	Ciptadent Lion Corp	Indonesia	?	$CaCO_3$	Na_2PO_3F 0.8%, NaF 0.01%	1101	1049	61
302*	Follow me Earth Chemical Japan	Malaysia	?	$CaCO_3$	Na_2PO_3F%?	?	167	55
303	Jaifun	Malaysia	?	DCPD	Na_2PO_3F%?	?	922	51
304	Systema Lion Corp	Japan	?	Silica	NaF%?	?	978	71
305	Sensodyne freshmint GSK	Australia	0309	Silica	NaF 0.32%	1448	1364	86
306	Colgate Kayu Sugi	China	0810	$CaCO_3$	Na_2PO_3F 1.1%	1451	1450	71
307	Colgate Fresh	Thailand	0810	Silica	NaF 0.221%	1000	962	74
308	Pepsodent Whitening Unilever	Indonesia	?	$CaCO_3$	Na_2PO_3F 0.8%	1056	1114	46
309	Sensitive Church & Dwight	Canada	?	?	NaF 0.243%	1099	1095	84
310	Siwaki F	Indonesia	?	$CaCO_3$	Na_2PO_3F 0.7%	924	1109	37
312	Colgate Total 12	Thailand	0710	Silica	NaF 0.22%	995	1023	72
313	Smile Up Lion Corp	Indonesia	?	Silica	Na_2PO_3F 0.8%, NaF 0.01%	1101	1035	81
314	Pepsodent Herbal Unilever	Indonesia	?	$CaCO_3$	Na_2PO_3F 0.8%	1056	1109	35
317	Colgate PCP regular flavour	Thailand	1109	DCPD	Na_2PO_3F 0.76%, NaF 0.1%	1455	1441	43
318	Colgate PCP Cool mint	Thailand	0610	DCPD	Na_2PO_3F 0.76%, NaF 0.1%	1455	1509	38
319	Pepsodent Gum Care Unilever	Indonesia	?	Silica	NaF 0.32%	1448	1312	75
320	Pepsodent Pencegah Unilever	Indonesia	?	$CaCO_3$	Na_2PO_3F 1.18%	1557	1659	60
321	Darlie Hawley & Hazel	China	0910	Silica	NaF%?	?	977	79
322	Sensodyne Gum Care GSK	Thailand	0209	Silica	NaF 0.221%	1000	1065	84
323*	Safi	Malaysia	0210	$CaCO_3$	Na_2PO_3F%?	?	266	31

*Not included in the calculation of the mean percentage of free fluoride.
DCPD, dicalciumphosphate dihydrate.

Table 4 Results of analyses of fluoride toothpastes purchased in Cambodia in August 2007 and analysed in November 2007

Lab no.	Label	Country of manufacture	Expiry date	Abrasives	F compound on label	ppm F calculated	Total ppm F in analysis	% free F of total in analysis
253	Colgate Max Fresh Cooling Crystals	Thailand	0510	Silica	NaF 0.22%	995	1001	93
254	Colgate Herbal	China	?	$CaCO_3$	Na_2PO_3F 0.76%	1003	1123	44
255	Colgate Herbal salt	Thailand	?	$CaCO_3$	Na_2PO_3F 0.76%	1003	979	100
256	Colgate Proven Cavity protection blue	Thailand	?	DCPD	Na_2PO_3F 0.76%	1003	1008	78
257	Colgate Proven Cavity protection green	Thailand	?	DCPD	Na_2PO_3F 0.76%	1003	1127	68
258	Colgate Double Cool Stripe	Thailand	?	?	NaF 0.22%	995	1029	91
259	Close up Unilever Fluo-active	Vietnam	0810	Silica	NaF 0.22%	995	950	100
260	Close up Unilever Milk Calcium	Vietnam	0210	Silica	NaF 0.22%	995	933	100
261	Close up Unilever Crystal White	Vietnam	?	Silica	NaF 0.22%	995	933	100
262	Darlie Full Fluoride Protection	China	?	DCPD	Na_2PO_3F%?	?	1015	46
263	Darlie Fresh's Brite	China	1009	Silica	NaF%?	?	1019	100
264	Darlie Double Action	Thailand	?	DCPD	Na_2PO_3F 0.76%	1003	1124	63
268	Lucky Kids Strawberry Flavor	Korea	?	CGP	Na_2PO_3F 0.76%	1003	1013	100
269	Pepsodent Unilever	?	0209	$CaCO_3$, CGP	Na_2PO_3F%?	?	1559	31

DCPD, dicalciumphosphate dihydrate; CGP, calcium glycerophosphate.

to further work by an ISO subcommittee. The methodology used in this study may thus differ from methods used by other laboratories or the manufacturers themselves

- Genuine and fake products: it has become increasingly complicated, if not impossible, to distinguish between a genuine and a counterfeit product. Labelling and packaging are all too often copied so accurately that even experts have difficulty in clearly identifying fake products. It is thus possible that some of the samples included in the study are in fact fake products. Although this would be an important finding with far-reaching consequences for consumers, national regulatory bodies and manufacturers, we can neither exclude nor confirm this assumption.

Despite these relevant limitations, the results strongly highlight critical problem areas related to fluoride toothpaste, particularly in countries in which regulatory and quality control systems for consumer products are weak.

Fluoride content and efficacy

The results showed that all but one of the fluoride toothpastes sampled from the Netherlands (both child and adult toothpastes) contained the declared amount

Table 5 Results of analyses of fluoride toothpastes purchased in Laos in August 2007 and analysed in November 2007

Lab no.	Label	Country of manufacture	Expiry date	Abrasives	F compound on label	ppm F calculated	Total ppm F in analysis	% free F of total in analysis
228	Colgate Total 12 hours whitening gel	Thailand	?	Silica	NaF 0.22%	995	961	98
229	Colgate Total 12 Fresh Stripe	Thailand	?	Silica	NaF 0.22%	995	987	95
230	Colgate Max Fresh with Cooling Crystals Peppermint Ice	Thailand	?	Silica	NaF 0.22%	995	982	100
231	Colgate Max Fresh with Cooling Crystals Minty Blast	Thailand	?	Silica	NaF 0.22%	995	936	100
232	Colgate Herbal salt	Thailand	?	$CaCO_3$	Na_2PO_3F 0.76%	1003	899	100
233	Colgate Proven Cavity protection-Great regular flavour blue	Thailand	?	DCPD	Na_2PO_3F 0.76%	1003	990	52
234	Colgate Proven Cavity protection-Fresh cool mint green	Thailand	?	DCPD	Na_2PO_3F 0.76%	1003	1120	49
235	Colgate Fresh Confidence A Verifiere	Thailand	?	?	NaF 0.221%	1000	944	100
236	Colgate Double Cool Stripe	Thailand	?	?	NaF 0.22%	995	989	100
237	Colgate Herbal white	Vietnam	?	$CaCO_3$	Na_2PO_3F 0.76%	1003	991	100
238	Sensodyne Original GSK	Thailand	0808	?	NaF 0.22%	995	971	96
239*	Sensodyne Cool Gel GSK	Thailand	0709	?	SnF_2%?	?	0	–
240	Darlie Double action License China	Thailand	?	TCP	Na_2PO_3F 0.76%	1003	1050	79
241	Darlie Tea care License China	Thailand	?	?	NaF 0.22%	995	967	98
244	Close up Unilever Milk Calcium	Vietnam	?	Silica	NaF 0.22%	995	979	96
245	Close up Unilever Menthol Chill	Vietnam	?	Silica	NaF 0.22%	995	966	87
246	Kodomo Lion Japan Children Xylitol Plus Toothpaste orange flavour	Thailand	?	?	NaF 0.11%	498	491	94
247	Kodomo Lion Japan Children Xylitol Plus Toothpaste grape flavour	Thailand	?	?	NaF 0.11%	498	492	94
248	Kodomo Lion Japan Children Gel Toothpaste bubble fruit flavour	Thailand	?	?	NaF 0.11%	498	472	100
249	Kodomo Lion Japan Children Gel Toothpaste strawberry flavour red	Thailand	?	?	Na_2PO_3F 0.38%	501	498	100
250	Kodomo Lion Japan Children Gel Toothpaste strawberry flavour pink	Thailand	?	?	NaF 0.11%	498	484	100

*Not included in the calculation of the mean percentage of free fluoride.
DCPD, dicalciumphosphate dehydrate; TCP, tricalciumphosphate.

Table 6 Results of analyses of fluoride toothpastes purchased in Suriname in August 2007 and analysed in November 2007

Lab no.	Label	Country of manufacture	Expiry date	Abrasives	F compound on label	ppm F calculated	Total ppm F in analysis	% free F of total in analysis
274	Colgate Maximum Cavity Protection	Dominica	0508	DCPD	Na_2PO_3F, NaF %?	?	1438	23
275	Colgate Proven Cavity Protection	Thailand	0508	DCPD	Na_2PO_3F 0.76%, NaF 0.1%	1455	1460	49
276	Colgate Herbal	Brazil	?	$CaCO_3$	Na_2PO_3F 1.1%	1451	1566	52
277	Colgate	China	?	DCP	Na_2PO_3F, NaF %?	?	1509	52
278	Maxam	China	?	Silica	Na_2PO_3F %?	?	1242	13
279	Maxam Strawberry Children toothpaste	China	?	DCP	Na_2PO_3F %?	?	1333	20
280	Maxam Gel Fresh	China	?	Silica	Na_2PO_3F %?	?	1093	100
281	Maxam Freshmint	China	?	CGP	Na_2PO_3F 0.8%	1056	1074	100
282*	Maxam Whitening	China	?	Silica	Na_2PO_3F %?	?	0	–
283*	Maxam Spearmint Flavor	China	?	Silica	Na_2PO_3F %?	?	0	–
285*	Maxam Triple Action contains	China	?	?	NaF%?	?	245	33
286	Pepsodent Bi-Calcio-Activ contains	Chile	?	$CaCO_3$	Na_2PO_3F 1.14%	1504	1614	15
287	Pepsodent Peppermint Unilever contains	Chile	?	Silica	Na_2PO_3F 0.8%	1056	1027	100
288	Pepsodent Unilever	?	?	$CaCO_3$	Na_2PO_3F 1000 ppm F	1000	991	28
289	Pepsodent Bi-calcio-Activ Unilever contains	Chile	?	$CaCO_3$	Na_2PO_3F 1.14%	1504	1567	13
290	Close-Up Septibucal Max Protection Unilever contains	Chile	1107	Silica	NaF 0.32%	1448	1475	98
291	Close-Up Septibucal Max Protection Unilever contains	Chile	0308	Silica	NaF 0.32%	1448	1422	100
292	Contente Plus Menta	Brazil	0907	$CaCO_3$	Na_2PO_3F 1500ppm F	1500	1591	39

*Not included in the calculation of the mean percentage of free fluoride.
DCPD, dicalciumphosphate dehydrate; DCP, dicalciumphosphate; CGP, calcium glycerophosphate.

Table 7 Mean percentage of free fluoride in Na_2PO_3F and NaF toothpastes with various abrasives from low-income countries and the number of these toothpastes with a free fluoride content of < 50% of total fluoride content

Type of toothpaste	*n*	Free F, %, mean ± SE	Toothpastes with < 50% free fluoride, *n*
Na_2PO_3F with calcium-containing abrasives	32	53.2 ± 4.3	16
Na_2PO_3F with silica or unknown abrasives	5	78.8 ± 19.1	1
NaF with silica	20	90.4 ± 2.4	0
NaF with unknown abrasives	10	95.7 ± 1.6	0

SE, standard error.

and type of fluoride and these complied with ISO Standard 11609. The picture was quite different for toothpastes from the other four countries, 8% of which contained either only a very low level of fluoride or no fluoride at all.

All samples from the Netherlands contained comparable amounts of total and free available fluoride (again with just one exemption), whereas toothpastes from the other four countries, particularly SMFP toothpastes, showed a low percentage of free available fluoride. Possible reasons for the differences in concentrations of free available fluoride include, but are not limited to:

- Toothpastes that are produced locally through subcontracted companies of global manufacturers may not be produced correctly or may be inadequately controlled for quality
- Low-cost toothpaste may use cheaper ingredients (abrasives) to increase profit margins
- Large batches of toothpaste nearing its expiry date may be sold by unscrupulous distributors in countries with weak controls and regulation
- Toothpaste may have a slow turnover depending on country, shop location, season etc., resulting in lengthy shelf life and sales near or beyond the expiration date
- High storage temperatures may have a negative influence on the stability of toothpaste in tropical regions
- Counterfeit products that imitate recognised brands may be of low quality.

Five of the six non-Dutch fluoride toothpastes that contained either very little or no fluoride were local brand products; the sixth claimed to be a multinational toothpaste brand. Counterfeit products and medicines are a rapidly growing global problem. The WHO defines a counterfeit medicine as: '…one which is deliberately and fraudulently mislabelled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products and counterfeit products may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredients or with counterfeit packaging'[14].

Although counterfeiting affects the toothpaste industry, the real extent of the problem is unknown. For example, counterfeit toothpaste falsely labelled as Colgate appeared on the market in Nigeria and Mozambique in 2007 and was found to contain potentially harmful concentrations of diethylene glycol[15,16]. It is therefore possible that some of the toothpastes from outside the Netherlands included in this study were indeed fake products. In this context it is worth mentioning that one toothpaste (no. 285), purchased in Suriname, was labelled as containing diethylene glycol, whereas five other toothpastes (nos. 286, 287, 289, 290 and 291) contained formaldehyde. In the European Union (EU), these chemicals are considered to be toxic and carcinogenic agents and are not allowed in toothpastes.

Although it is possible to maintain fluoride stability in toothpastes for > 3 years, studies have shown this is not always the case in commercially available toothpastes[17,18]. The belief that SMFP has the advantage of being compatible with chalk-based abrasives is still widespread[19]. A paper on the effective use of fluorides in the *Bulletin of the WHO*[20] suggested precipitated calcium carbonate as the abrasive agent of choice because of its low cost and availability in developing countries. Reference was made to a clinical trial conducted under the auspices of the WHO in Indonesia. However, the paper[21] describing this clinical trial admitted that calcium carbonate was not optimally compatible with the fluoride source in the toothpaste and argued that the formation of CaF_2 in the SMFP toothpaste was prevented by the addition of a stabiliser to the toothpaste. Notwithstanding this latter statement the present study challenges the claimed stability of SMFP toothpastes with calcium-containing abrasives because 46% of the SMFP toothpastes from countries outwith the Netherlands contained < 50% free available fluoride. These findings are supported by several other papers. A study in Brazil showed that the percentage of free available fluoride in nine fresh SMFP toothpastes with calcium-containing abrasives was significantly lower than the mean percentage of free available fluoride in seven NaF toothpastes containing silica (mean free available fluoride: 81% in SMFP *vs.* 98% in NaF toothpastes)[22]. Toothpastes lose free available fluoride as they age and with increasing temperatures, particularly SMFP toothpastes with calcium-containing abrasives[22–25]. Studies have shown toothpastes to lose an average of 25% of free available fluoride after one year of storage at 22 °C, and a mean of about 35% of free available fluoride after one year of storage at 29 °C[23,25].

The literature indicates the existence of a statistically significant positive relationship between the caries

protective effect and fluoride content in toothpastes with > 1100 ppm F[26]. Concentrations of 440 ppm F, 500 ppm F and 550 ppm F and below showed no statistically significant effect on dental caries compared with placebo[27,28]. However, the conclusion that the efficacy of toothpastes containing 440–550 ppm F does not significantly differ from that of placebo is based on the outcomes of only two trials, whereas the claim that toothpastes with 1500 ppm F had a preventive effect superior to that of toothpastes with 1000 ppm F is based on the findings of a considerable number of trials. Nevertheless, the literature does not provide conclusive information on which concentration of free available fluoride in toothpaste exerts the best anti-caries efficacy. Consequently, national and international guidelines for cosmetic products primarily deal with the total fluoride content of toothpastes and these state that this should not exceed 1500 ppm F. The only exception are the guidelines of the US Food and Drug Administration, which state that NaF and SMFP toothpastes containing 850–1150 ppm total fluoride should contain ≥ 650 ppm and ≥ 800 ppm available fluoride, respectively. The rationale for these values remains obscure[29]. The ISO Standard 11609 currently refers only to the total fluoride content of toothpaste and does not address the need to indicate the content of free available fluoride in toothpaste, although this is an essential requirement for anti-caries efficacy[30].

The absence of requirements based on definitions of fluoride toothpaste efficacy in many current national and international guidelines leads to a situation in which even a toothpaste that contains only minimal quantities of free available fluoride would be considered a fluoride dentifrice, despite the lack of any anti-caries benefit.

Content declaration and labelling

Most of the toothpastes from the four non-Dutch countries did not indicate an expiry date on the package, and six of the 21 declared an expiry date of < 1 year from purchase. Information on expiry date is important because manufacturers do not guarantee the quality of toothpaste after expiry. Failure to provide an expiry or manufacturing date represents the withholding of essential information about the efficacy of the product from consumers. In fact, ISO Standard 11609 defines minimum labelling requirements that relate to expiry date, a full declaration of the fluoride type and amount contained and the type of abrasive. However, the large majority of fluoride toothpastes bought for the study in countries other than the Netherlands did not meet such requirements.

CONCLUSIONS

Toothpastes in the Netherlands have full anti-caries efficacy in accordance with declared total fluoride content. Many toothpastes in this sample from countries outwith the Netherlands, including those labelled as major brands, may have questionable anti-caries efficacy as a result of a lack of free available fluoride. Possible causes of this lack are discussed in this paper.

Given that fluoride toothpaste remains the most widespread and significant form of fluoride application and is used worldwide for the reduction and control of dental caries, it is essential that fluoride toothpastes contain sufficient free available fluoride to assure their effectiveness. This study has highlighted problem areas relating to quality control, standard setting and compliance with existing standards for fluoride toothpaste. Weak quality control systems and lack of compliance on the part of manufacturers may put consumers, particularly in low- and middle-income countries, at further disadvantage or even risk. Appropriate quality control of toothpaste requires technical capacity, but also the political will and commitment to establish strong national drug and consumer product regulatory authorities. Such bodies would also be responsible for ensuring that products on the market comply with minimum labelling and packaging requirements, such as ISO Standard 11609. An additional problem regarding the quality of toothpaste concerns the almost total neglect of the importance of free available fluoride. It is recommended and overdue that international standards are defined in order to determine what constitutes effective fluoride toothpaste.

Recommendations for health communication

As long as the quality of toothpastes available in many countries cannot be ensured, it is important for health communication and consumer advocacy to suggest these simple guidelines:

- Always check the expiry date of toothpaste
- Do not purchase a toothpaste that has expired or that does not show an expiry date
- Silica-based fluoride toothpaste without any calcium-containing abrasive is more likely to have full anti-caries efficacy
- SMFP toothpaste is less likely to be fully effective against dental caries unless it has been recently produced (three years before the expiry date).

Conflicts of interest

None declared.

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