



## Clinical trial results: Fluoride in saliva during and after use of high-fluoride toothpaste Summary

EudraCT number	2020-000213-33
Trial protocol	DK
Global end of trial date	23 February 2021

### Results information

Result version number	v1 (current)
This version publication date	03 February 2022
First version publication date	03 February 2022

### Trial information

#### Trial identification

Sponsor protocol code	14012020
-----------------------	----------

#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Aarhus University
Sponsor organisation address	Vennelyst Boulevard 9, Aarhus, Denmark, 8000
Public contact	Line Staun Larsen, Department of Dentistry and Oral Health, +45 87168479, line.staun@dent.au.dk
Scientific contact	Line Staun Larsen, Department of Dentistry and Oral Health, +45 87168479, line.staun@dent.au.dk

Notes:

#### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 January 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 February 2021
Global end of trial reached?	Yes
Global end of trial date	23 February 2021
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To explore how much regular brushing with 5,000 ppm fluoride toothpaste (Duraphat 5mg/g toothpaste) would elevate the salivary fluoride concentration compared to brushing with 1,450 ppm fluoride toothpaste, and to study how fast the salivary fluoride concentration would return to baseline levels following resumption of brushing with 1,450 ppm fluoride toothpaste.

Protection of trial subjects:

N/A

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	01 September 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 50
Worldwide total number of subjects	50
EEA total number of subjects	50

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	50
From 65 to 84 years	0

85 years and over	0
-------------------	---

## Subject disposition

### Recruitment

Recruitment details:

Students from Aarhus University who volunteered based on posters in campus canteens during the period from August 2020 to January 2021.

### Pre-assignment

Screening details:

Adults ( $\geq 18$  year), at least 20 teeth, non-pregnant and non-nursing, an unstimulated salivary flow rate of at least 1 ml/5 min.

### Period 1

Period 1 title	Overall trial: trial & wash-out phase (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst

Blinding implementation details:

Identical tubes; toothpaste kits (one kit for each participant) were prepared and labelled by authorised pharmaceutical staff at the Hospital Pharmacy Central Denmark Region.

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Test arm

Arm description:

Trial phase: Participants used Duraphat 5mg/g tandpasta (toothpaste) twice daily for three weeks.  
Wash-out phase: Participants used 1,450 ppm fluoride toothpaste (Colgate® Fresh Gel; a cosmetic product, not medicine) twice daily for two weeks.  
(The phases were consecutive.)

Arm type	Experimental
Investigational medicinal product name	Duraphat 5mg/g tandpasta
Investigational medicinal product code	
Other name	Duraphat® 5000 ppm Fluoride Toothpaste
Pharmaceutical forms	Toothpaste
Routes of administration	Oral use

Dosage and administration details:

Toothbrushing twice daily (morning and evening) with 1 g of toothpaste.

Investigational medicinal product name	Colgate® Fresh Gel; a cosmetic product, not medicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Toothpaste
Routes of administration	Oral use

Dosage and administration details:

Toothbrushing twice daily (morning and evening) with 1 g of toothpaste.

<b>Arm title</b>	Control arm
------------------	-------------

Arm description:

Trial phase: Participants used 1,450 ppm fluoride toothpaste (Colgate® Fresh Gel; a cosmetic product, not medicine) twice daily for three weeks.  
Wash-out phase: Participants continued to use 1,450 ppm fluoride toothpaste twice daily for two weeks.  
(The phases were consecutive.)

Arm type	Control arm
----------	-------------

Investigational medicinal product name	Colgate® Fresh Gel; a cosmetic product, not medicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Toothpaste
Routes of administration	Oral use

Dosage and administration details:

Toothbrushing twice daily (morning and evening) with 1 g of toothpaste.

<b>Number of subjects in period 1</b>	Test arm	Control arm
Started	25	25
Completed	24	24
Not completed	1	1
Covid19-related circumstances	1	1

## Baseline characteristics

### Reporting groups

Reporting group title	Test arm
Reporting group description:	
Trial phase: Participants used Duraphat 5mg/g tandpasta (toothpaste) twice daily for three weeks. Wash-out phase: Participants used 1,450 ppm fluoride toothpaste (Colgate® Fresh Gel; a cosmetic product, not medicine) twice daily for two weeks. (The phases were consecutive.)	
Reporting group title	Control arm
Reporting group description:	
Trial phase: Participants used 1,450 ppm fluoride toothpaste (Colgate® Fresh Gel; a cosmetic product, not medicine) twice daily for three weeks. Wash-out phase: Participants continued to use 1,450 ppm fluoride toothpaste twice daily for two weeks. (The phases were consecutive.)	

Reporting group values	Test arm	Control arm	Total
Number of subjects	25	25	50
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	22.4	23.5	
standard deviation	± 1.5	± 2.2	-
Gender categorical Units: Subjects			
Female	20	17	37
Male	5	8	13

## End points

### End points reporting groups

Reporting group title	Test arm
Reporting group description: Trial phase: Participants used Duraphat 5mg/g tandpasta (toothpaste) twice daily for three weeks. Wash-out phase: Participants used 1,450 ppm fluoride toothpaste (Colgate® Fresh Gel; a cosmetic product, not medicine) twice daily for two weeks. (The phases were consecutive.)	
Reporting group title	Control arm
Reporting group description: Trial phase: Participants used 1,450 ppm fluoride toothpaste (Colgate® Fresh Gel; a cosmetic product, not medicine) twice daily for three weeks. Wash-out phase: Participants continued to use 1,450 ppm fluoride toothpaste twice daily for two weeks. (The phases were consecutive.)	

### Primary: Salivary fluoride at day 0 (baseline) of the trial phase

End point title	Salivary fluoride at day 0 (baseline) of the trial phase <sup>[1]</sup>
End point description: Saliva sampling days during the experimental period: day 0 (baseline), 7, 10, 14, 21, 22, 23, 24, 28 and 35. According to phases: day 0, 7, 10, 14 and 21 of the trial phase and day 1, 2, 3, 7 and 14 of the wash-out phase. Day 21 of the trial phase is identical to day 0 in the wash-out phase.	
End point type	Primary
End point timeframe: Day 0 (baseline) of the trial phase.	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Scientific paper, incl. detailed statistical analysis description, will be uploaded after publication.

End point values	Test arm	Control arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: parts per million				
geometric mean (confidence interval 95%)	0.016 (0.012 to 0.021)	0.014 (0.011 to 0.019)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Salivary fluoride at day 7 of the trial phase

End point title	Salivary fluoride at day 7 of the trial phase <sup>[2]</sup>
End point description:	
End point type	Primary

End point timeframe:

Day 7 of the trial phase.

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Scientific paper, incl. detailed statistical analysis description, will be uploaded after publication.

End point values	Test arm	Control arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: parts per million				
geometric mean (confidence interval 95%)	0.035 (0.025 to 0.048)	0.020 (0.014 to 0.029)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Salivary fluoride at day 10 of the trial phase

End point title Salivary fluoride at day 10 of the trial phase<sup>[3]</sup>

End point description:

End point type Primary

End point timeframe:

Day 10 of the trial phase.

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Scientific paper, incl. detailed statistical analysis description, will be uploaded after publication.

End point values	Test arm	Control arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: Parts per million				
geometric mean (confidence interval 95%)	0.036 (0.024 to 0.052)	0.021 (0.015 to 0.030)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Salivary fluoride at day 14 of the trial phase

End point title Salivary fluoride at day 14 of the trial phase<sup>[4]</sup>

End point description:

End point type Primary



End point timeframe:

Day 14 of the trial phase.

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Scientific paper, incl. detailed statistical analysis description, will be uploaded after publication.

End point values	Test arm	Control arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: parts per million				
geometric mean (confidence interval 95%)	0.032 (0.021 to 0.049)	0.017 (0.012 to 0.024)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Salivary fluoride at day 21 of the trial phase (end of trial phase)

End point title	Salivary fluoride at day 21 of the trial phase (end of trial phase) <sup>[5]</sup>
-----------------	--

End point description:

End point type	Primary
----------------	---------

End point timeframe:

Day 21 of trial phase.

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Scientific paper, incl. detailed statistical analysis description, will be uploaded after publication.

End point values	Test arm	Control arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: parts per million				
geometric mean (confidence interval 95%)	0.044 (0.029 to 0.066)	0.023 (0.015 to 0.034)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Salivary fluoride at day 1 of the wash-out phase

End point title	Salivary fluoride at day 1 of the wash-out phase <sup>[6]</sup>
-----------------	---

End point description:

End point type	Primary
----------------	---------

End point timeframe:

Day 1 of the wash-out phase.

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Scientific paper, incl. detailed statistical analysis description, will be uploaded after publication.

End point values	Test arm	Control arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: parts per million				
geometric mean (confidence interval 95%)	0.025 (0.016 to 0.039)	0.015 (0.011 to 0.020)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Salivary fluoride at day 2 of the wash-out phase

End point title Salivary fluoride at day 2 of the wash-out phase<sup>[7]</sup>

End point description:

End point type Primary

End point timeframe:

Day 2 of the wash-out phase.

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Scientific paper, incl. detailed statistical analysis description, will be uploaded after publication.

End point values	Test arm	Control arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: parts per million				
geometric mean (confidence interval 95%)	0.023 (0.014 to 0.036)	0.019 (0.014 to 0.025)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Salivary fluoride at day 3 of the wash-out phase

End point title Salivary fluoride at day 3 of the wash-out phase<sup>[8]</sup>

End point description:

End point type Primary

End point timeframe:

Day 3 of the wash-out phase.

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Scientific paper, incl. detailed statistical analysis description, will be uploaded after publication.

End point values	Test arm	Control arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: parts per million				
geometric mean (confidence interval 95%)	0.024 (0.016 to 0.038)	0.018 (0.013 to 0.025)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Salivary fluoride at day 7 of the wash-out phase

End point title	Salivary fluoride at day 7 of the wash-out phase <sup>[9]</sup>
-----------------	---

End point description:

End point type	Primary
----------------	---------

End point timeframe:

Day 7 of the wash-out phase.

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Scientific paper, incl. detailed statistical analysis description, will be uploaded after publication.

End point values	Test arm	Control arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: parts per million				
geometric mean (confidence interval 95%)	0.023 (0.016 to 0.034)	0.025 (0.016 to 0.039)		

## Statistical analyses

No statistical analyses for this end point

### Primary: Salivary fluoride at day 14 of the wash-out phase (end of the wash-out phase)

End point title	Salivary fluoride at day 14 of the wash-out phase (end of the wash-out phase) <sup>[10]</sup>
-----------------	---

End point description:

End point type	Primary
----------------	---------

End point timeframe:

Day 14 of the wash-out phase.

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Scientific paper, incl. detailed statistical analysis description, will be uploaded after publication.

End point values	Test arm	Control arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: parts per million				
geometric mean (confidence interval 95%)	0.025 (0.017 to 0.036)	0.016 (0.011 to 0.023)		

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

During the trial, from inclusion of the first participant to the end of trial.

Assessment type	Systematic
-----------------	------------

### Dictionary used

Dictionary name	N/A
-----------------	-----

Dictionary version	1
--------------------	---

### Reporting groups

Reporting group title	Test arm
-----------------------	----------

Reporting group description:

Trial phase: Participants used Duraphat 5mg/g tandpasta (toothpaste) twice daily for three weeks.  
Wash-out phase: Participants used 1,450 ppm fluoride toothpaste (Colgate® Fresh Gel; a cosmetic product, not medicine) twice daily for two weeks.  
(The phases were consecutive.)

Reporting group title	Control arm
-----------------------	-------------

Reporting group description:

Trial phase: Participants used 1,450 ppm fluoride toothpaste (Colgate® Fresh Gel; a cosmetic product, not medicine) twice daily for three weeks.  
Wash-out phase: Participants continued to use 1,450 ppm fluoride toothpaste twice daily for two weeks.  
(The phases were consecutive.)

Serious adverse events	Test arm	Control arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Test arm	Control arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	
Vascular disorders			
Migraine	Additional description: A participant, with no history of migraines, reported to have had a migraine for two days (day 12 and 13 in the trial phase).		
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Rash	Additional description: Skin rash in the ear, neck and thorax areas developed two weeks into the trial phase.		

subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	
occurrences (all)	1	0	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported