RESEARCH ARTICLE

# Fluoride release from two types of fluoride-containing orthodontic adhesives: Conventional versus resin-modified glass ionomer cements—An in vitro study

Yasemin Dziuk[1], Sachin Chhatwani[1]*, Stephan C. Möhlhenrich[1], Sabrina Tulka[2], Ella A. Naumova[3], Gholamreza Danesh[1]

1 Department of Orthodontics, Faculty of Health, University of Witten/Herdecke, Witten, Germany, 2 Faculty of Health, Institute for Medical Biometry and Epidemiology, University of Witten/Herdecke, Witten, Germany, 3 Faculty of Health, Department of Biological and Material Sciences in Dentistry, University of Witten/Herdecke, Witten, Germany

☯ These authors contributed equally to this work.
* sachin.chhatwani@uni-wh.de

## Abstract

### Introduction

Development of white spot lesions (WSLs) during orthodontic treatment is a common risk factor. Fixation of the orthodontic appliances with glass ionomer cements could reduce the prevalence of WSL's due to their fluoride release capacities. The purpose of this study was to evaluate differences of fluoride release properties from resin-modified and conventional glass ionomer cements (GICs).

### Methods

The resin-modified GICs Fuji ORTHO LC (GC Orthodontics), Meron Plus QM (VOCO), as well as the conventional GICs Fuji ORTHO (GC Orthodontics), Meron (VOCO) and Ketac Cem Easymix (3M ESPE) were tested in this study. The different types of GICs were applied to hydroxyapatite discs according to the manufacturer's instructions and stored in a solution of TISAB III (Total Ionic Strength Adjustment Buffer III) and fluoride-free water at 37˚C. Fluoride measurements were made after 5 minutes, 2 hours, 24 hours, 14 days, 28 days, 2 months, 3 months and 6 months. One factor analysis of variance (ANOVA) was used for the overall comparison of the cumulative fluoride release (from measurement times of 5 minutes to 6 months) between the different materials with the overall level of significance set to 0.05. Tukey's post hoc test was used for post hoc pairwise comparisons in the cumulative fluoride release between the different materials.

### Results

The cumulative fluoride release (mean ± sd) in descending order was: Fuji ORTHO LC (221.7 ± 10.29 ppm), Fuji ORTHO (191.5 ± 15.03 ppm), Meron Plus QM (173.0 ± 5.89 ppm), Meron (161.3 ± 7.84 ppm) and Ketac Cem Easymix (154.6 ± 6.09 ppm) within 6 months.

Analysis of variance detected a significant difference in the cumulative fluoride release between at least two of the materials (rounded p-value < 0.001). Pairwise analysis with Tukey's post hoc test showed a significant difference in the cumulative fluoride release for all the comparisons except M and MPQM (p = 0.061) and KCE and M (p = 0.517).

## Conclusion

Fluoride ions were released cumulatively over the entire test period for all products. When comparing the two products from the same company (Fuji ORTHO LC vs. Fuji ORTHO from GC Orthodontics Europe GmbH and Meron Plus QM vs. Meron from VOCO GmbH, Mannheim, Germany), it can be said that the resin-modified GICs have a higher release than conventional GICs. The highest individual fluoride release of all GICs was at 24 hours. A general statement, whether resin-modified or conventional GICs have a higher release of fluoride cannot be made.

## Introduction

Multi-bracket (MB) treatment during orthodontic treatment is commonly associated with the development of white spot lesions (WSL) with an occurrence mostly reported between 24% and 72,9% [1], but can even vary between 2% up to even 97% [2]. In comparison, the prevalence of WSL's in patients without orthodontic treatment is only between 11% and 24% [3]. Most of the time lateral incisors and canines are affected by WSL's [4] and usually occur around the orthodontic fixed appliances [5].

White spot lesions are demineralizations that occur due to bacterial plaque activity and metabolism of carbohydrates resulting in an acid release [6], thus demineralize the dental hard tissue [7] and appear as a patch on the surface of the tooth [8]. Bands, brackets and arches increase plaque retention [2], block access to those plaque retaining areas and complicate adequate cleaning [9].

Therefore it is very important to implement and improve an effective remineralization mechanism [6], which counteracts this process, inhibits acid production and improves resistance to demineralization [7].

Due to their caries-preventive effect through the release of fluoride ions, glass ionomer cements are already widely used for the fixation of orthodontic bands [10] and could be an aid in prevention of white spot lesions.

In restorative materials, the fluoride released has an effective zone of 1 mm [11] and can inhibit demineralization up to 7 mm from the edge of the glass ionomer cement [12]. GICs are capable of maintaining a fluoride concentration of 0.03 ppm in oral saliva after one year [13]. Fluoride release rates in the range of 200–300 $\mu g/cm^2$ per month are considered sufficient to inhibit enamel demineralization [14].

Many studies only cover a time period of one day to 2 months [6, 15, 16]. However, there is little to no information on how fluoride release changes, especially in the first hours, after one month of the so-called "early burst" phase and the long-term release in the range of up to 6 months.

The purpose of this study was the evaluation of the continuous fluoride release of different GICs over a period of 6 months and to compare the differences between resin-modified GICs and conventional GICs.

## Materials and method

In the present study, five different GICs were investigated. The first two groups were resin-modified GICs, groups 3 to 5 were made up of conventional GICs. Group 6 represents a compomer and like group 7 served as an untreated control group (Table 1).

Flouride–free hydroxyapatite discs (HiMed Inc., Old Bethpage, USA) were used as carrier discs (5mm x 2mm) for the test materials. To control the exact amount of material applied an analytical balance was used (analytical balance, Secura CPA124S, Sartorius AG, Goettingen, Germany). On average 0,025g of test material was used on each disc. If there was a notable difference in weight of the test specimen the process had to be repeated.

The test material was applied to the carrier discs according to manufacturer instructions (Table 1). Surface conditioning was only necessary for Fuji Ortho (FO) with Fuji Ortho Conditioner (GC Orthodontics Europe GmbH, Breckerfeld, Germany). No material was applied to the carrier discs of the seventh group.

Sample size consisted of ten test specimens per group. The selection of n = 10 per group was based on previously published studies [17–20].

**Table 1. Materials examined in this study.**

| Group | Product | Material compostion | Company | Lot number | Product application |
|---|---|---|---|---|---|
| 1 | Fuji ORTHO LC (FOLC) (resin-modified GIC) | Liquid: 2-hydroxyethyl methacrylate 25–50%, Tartaric acid 5–10%, 2-Hydroxy-1 and 3-dimethacryloxypropane 1–5%, 7, 7, 9 (or 7, 9, 9)–Trimethyl-4, 13 –dioxo-3, 14-dioxa-5,12-diazahexadecane-1, 16-diylbismethacrylate 1–5%<br><br>Powder: Oxides, silanes | GC Orthodontics Europe GmbH, Breckerfeld, Germany | Liquid: 1804021<br><br>Powder: 1804051 | etching: optional surface conditioning:-mixing ratio:1 spoon / 2 drops of liquid (3.0g / 1.0g) processing time: 3min setting time: 5 1/2min light curing time: 40s |
| 2 | Meron Plus QM (MPQM) (resin-modified GIC) | Fluoroaluminosilicate glass 50–100%, hydroxypropyl methacrylate 10–25%, glycerine dimethacrylate 5–10%, Urethane dimethacrylate 2.5–5% | VOCO GmbH, Mannheim, Germany | 1904080 | etching:—surface conditioning:- mixing ratio:—processing time: 2min setting time: 4 1/2min light curing time: optional 5–10s |
| 3 | Fuji ORTHO (FO) (conventional GIC) | Liquid: 2-hydroxyethyl methacrylate (HEMA) 25–50%, polybasic carboxylic acid 5–10%, urethane dimethacrylate (UDMA) 1–5% Powder: confidential business information | GC Orthodontics Europe GmbH, Breckerfeld, Germany | Liquid: 808031<br><br>Powder: 1808101<br><br>Conditioner: 1807101 | etching: optional surface conditioning: Fuji Conditioner 20s, rinse, blow and dry mixing ratio: 1 spoon / 2 drops of liquid (3.0g / 1.0g) processing time: 3min setting time:5 1/2min light curing time:- |
| 4 | Meron (M) (conventional GIC) | Liquid: L-tartaric acid 10–15%<br><br>Powder: Fluoroaluminosilicate glass 50–100%, Polyacrylic acid 25–50% | VOCO GmbH, Mannheim, Germany | Liquid: 1848330<br><br>Powder: 1851411 | etching:—surface conditioning:—mixing ratio: 1 measuring spoon / 1 drop of liquid (3.0g / 1.0g) processing time: 3min setting time: 5 – 7min light curing time:- |
| 5 | Ketac Cem Easymix (KCE) (conventional GIC) | Liquid: Wasser 80–90%, Weinsäure < 20%<br><br>Pulver: Polycarbonsäure 20–25 Gew-%,Glaspulver 70–80 Gew-% | 3M ESPE GmbH, Germany | Liquid: 4328913<br><br>Powder: 4303869 | etching: -surface conditioning: -mixing ratio: 1 measuring unit powder / 2 drops of liquid (3.8g / 1.0g) processing time: 3min setting time: 7min light curing time:- |
| 6 | Ultra Band Lok (UBL) (compomer) | BisGMA 10–30%, Barium Monoxide 3,90–6,51%, 2-Hydroxyethyl Methacrylate 1–5%, 3-(Trimethoxysilyl)propyl-2-Methyl-2-Propenoic Acid 0,26–3,90%, SG-355RG4000CMP3 30–50% | Reliance Orthodontic Products Inc., Itasca, USA | - | etching:-surface conditioning: -mixing ratio:-processing time:-setting time:-light curing time:30s |
| 7 | hydroxyapatite discs | hydroxyapatite | HiMed Inc., Old Bethpage, USA | - | not applicable |

GIC = glass ionomer cement g = gram/grams s = second/seconds min = minute/minutes.

resin-modified glass ionomer cements (group 1 and 2); conventional glass ionomer cements (group 3–5); control groups (group 6 and 7).

The storage solution in which the carrier discs were placed contained a TISAB III solution (Total Ionic Strength Adjustment Buffer, Thomas Scientific, Swedesboro, USA) with bi-distilled water (Megro GmbH & Co. KG, Wesel, Germany) with a mixing ratio of 5%:95%.

For measurements, TISAB III was used to maintain a low pH value of 5–5.5 with constant ionic strength and to unmask the fluoride ions of the samples.

The fluoride measurement was performed with a fluoride electrode (Orion 9609BNWP, Thermo Fisher Scientific Inc., Chelmsford, USA). The measurement was repeated five times for each test specimen to prevent fluctuation. Calibration of the electrode is essential to obtain reliable measured values. For this reason, four fluoride standard solutions were prepared with sodium fluoride and diluted TISAB III containing fluoride of 0.38, 3.8, 38 and 380ppm.

Thereby a two-point calibration could be carried out with solutions containing an exact ion concentration. If the measured values deviated by more than 5%, the calibration had to be restarted. The required slope of the electrode in mV mode had to be between 56mV and 60mV. A further solution served additionally as a precision control to ensure consistency of the electrode on each measuring day. This precision control solution was obtained in preliminary tests, in which a pool of cryotubes containing a solution with known fluoride ion concentration was created. They were split up into two separate pools P1 and P2, consisting of a group with low and high amounts of fluoride (P1: 0,6566 ppm, P2: 16,7 ppm).

The 70 test specimens for this study were each kept in an individually labeled cryotube with 1.5ml diluted TISAB III and were stored in an incubator (WTB Binder, Tuttlingen, Germany) at 37˚C for the entire duration of the experiment (MELAG Medizintechnik oHG, Berlin, Germany) except for measurement procedures. Fluoride ion measurements were carried out at the following times:

After 5 minutes, 2 hours, 24 hours, 14 days, 4 weeks, 2 months, 3 months and 6 months.

At each measurement time, the carrier discs were placed in new cryotubes containing 1.5ml diluted TISAB III and were replaced in the incubator at 37˚C.

After separation of the carrier discs, the old cryotubes were placed in a vortex mixer for 10 seconds and subsequently 500µl of the solution was removed with a pipette and inserted in an empty test tube (4ml) for the measurement of the fluoride ion concentration. This procedure was repeated five times per tube to detect any fluctuations.

The fluoride ion electrode was rinsed with bi-distilled water before and after every contact with the tested solution.

Descriptive analysis for the primary endpoint (cumulative fluoride release) was performed with boxplots and nonparametric location parameters (minimum, first quartile, median, third quartile, maximum) supplemented with arithmetic mean and standard deviation of the cumulative fluoride release for every material.

One factor analysis of variance (ANOVA) was used for the overall comparison of the cumulative fluoride release (from measurement times 5 minutes to 6 months) between the different materials (FOLC, MPQM, FO, M, KCE) as primary statistical analysis of this study with the overall level of significance set to 0.05. As there was no fluoride release for UBLOK and the control these two materials were excluded from the ANOVA (see results section). Levene's test was used to assess the equality of variances (a p-value greater than 0.05 indicates that the equality of variances cannot be rejected). Quantile-quantile plots (QQ-Plots) will be used for comparing the probability distribution of data with the normal distribution. Tukey's post hoc test was used for post hoc pairwise comparisons in the cumulative fluoride release between the different materials. Results will be presented with difference in means with standard deviation and adjusted p-values. Additional descriptive analysis for every measuring time is presented with means and line plots. All the statistical analysis of data was done with R Version 3.6.0 (Software R Core Team, 2019).

## Results

After 5 minutes a fluoride ion release could already be observed for FOLC with 2.14 ± 0.47 ppm and KCE with 28.97 ± 1.76ppm.

A rise in fluoride at measuring time after 2 hours ion release was observed for all test materials except for KCE and the control groups. After 24 hours all materials with fluoride release (MPQM, FOLC, FO, M, KCE) had the highest individual fluoride ion release. FO achieved the highest value at this time of measurement with a release of 62.06 ± 13.45 ppm whereas the lowest value was seen for KCE with 31.66 ± 2.48 ppm. Between 24 hours and 14 days, a clinically relevant decrease in fluoride ion release was observed for every material with fluoride release. In the following period from 4 weeks to 6 months a steady fluoride release plateau was established (Fig 2). There were only relatively small fluctuations within the intervals in the individual groups. The highest fluctuations were found for MPQM and the lowest fluctuations for M.

Analysis of the control groups revealed a fluoride ion release of UBL after 5 minutes of 0.046 ± 0.02 ppm while the untreated control group had a delivery of 0.059 ± 0.01 ppm. After 2 hours the untreated control showed a small increase to 0.1 ± 0.25 ppm, with a subsequent decrease to a level of 0.01 ± 0.00 ppm after 24 hours. After 14 days to 6 months changes in fluoride ion release for UBL and the untreated control group remained negligible. Compared to the other materials (MPQM, FOLC, FO, M, the control groups didn't show any relevant fluoride release (Fig 1).
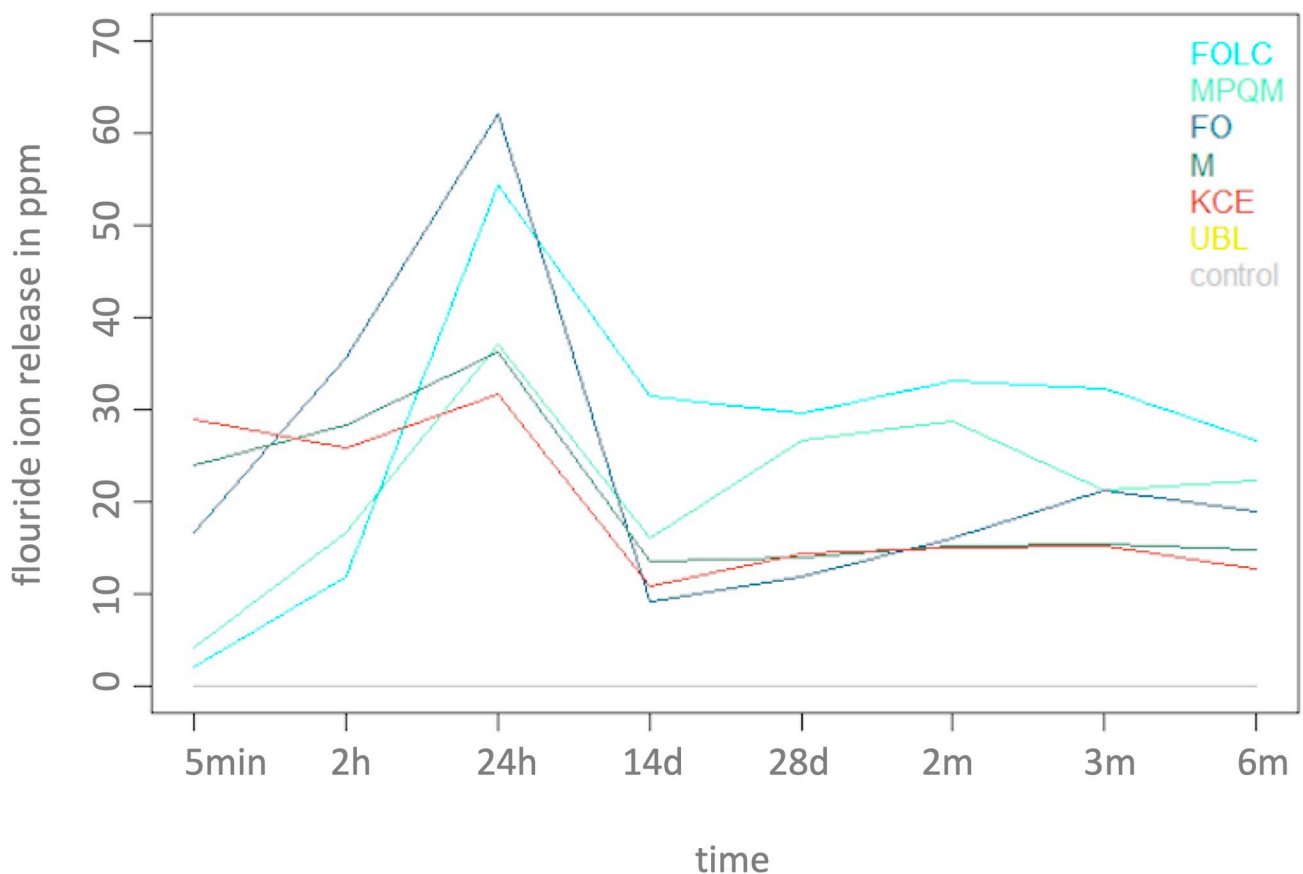


**Fig 1. Individual release of fluoride ions (in ppm) at the individual times 5 minutes—6 months of groups 1–7.** ppm = parts per million; min = minute/minutes; h = hours; d = days; m = months.

https://doi.org/10.1371/journal.pone.0247716.g001
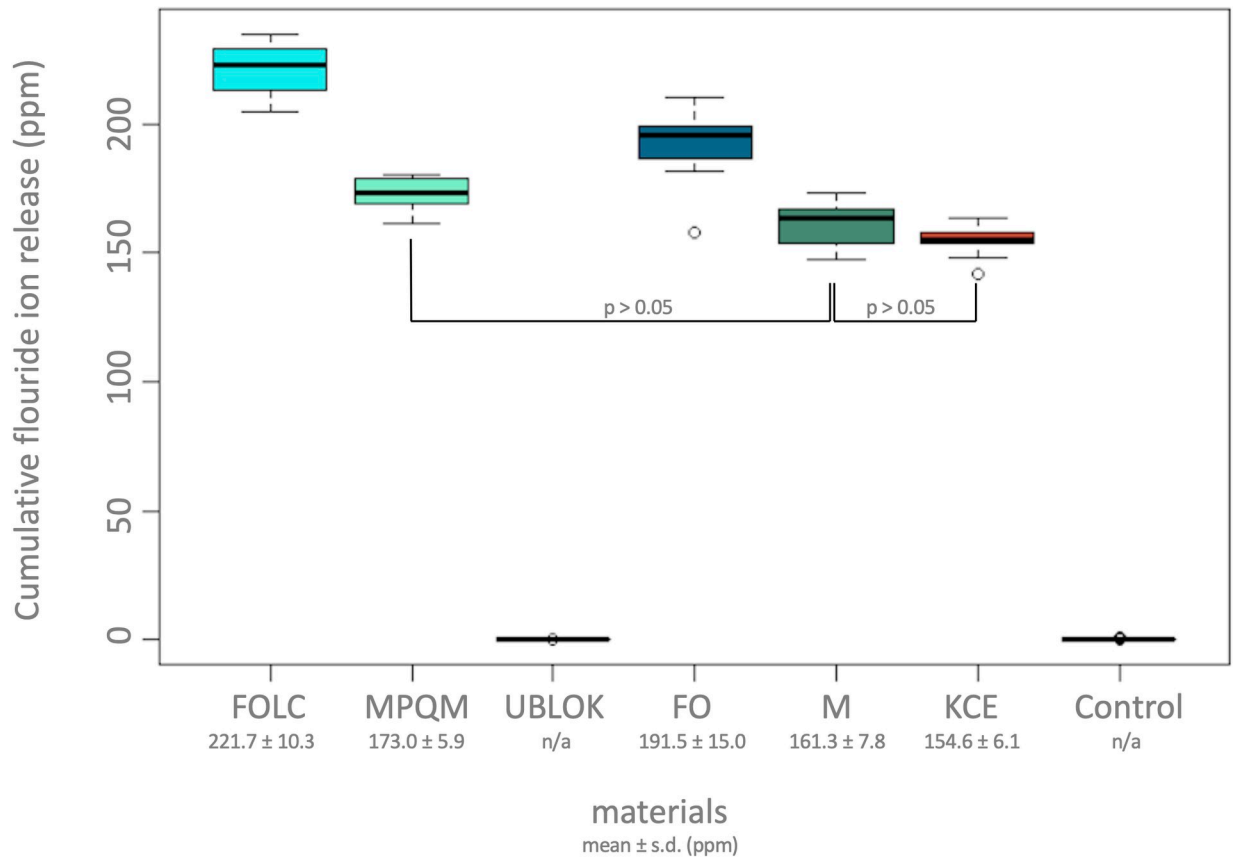
**Fig 2. Boxplots of the cumulative fluoride release over all measurement points for all materials (FOLC, MPQM, UBLOK, FO, M, KCE, Control).** s.d. = standard deviation; ppm = parts per million; p-value given for Tukey´s post hoc test.

FOLC and MPQM show a similar pattern of fluoride ion release over time with a peak after 24 hours, declining after 14 days and then building a plateau. This additional analysis was executed by descriptive means. No time dependent statistical tests were performed for the comparison of FOLC and MPQM. But post hoc test in the primary analysis of this study showed a significant cumulative fluoride release over time ($p < 0.001$) (Fig 1).

Primary analysis was done via one factor (material) analysis of variance for the cumulative fluoride release. The following materials were included in this analysis: FOLC, MPQM, FO, M, KCE. The control material as well as UBLOK were excluded from the analysis of variance due to the missing fluoride release (see above). The normality-assumption of the data was not refused as no qq-plot showed great or systematic deviations from the baseline. A significant difference in total cumulative fluoride ion release between at least two of the investigated materials FOLC, MPQM, FO, M and KCE could be found ($p < 0.001$).

Following pairwise comparisons with Tukey's post hoc test showed no significant difference ($p > 0.05$) in cumulative fluoride release between Meron and Meron Plus QM (Fig 1). All other materials had statistically different cumulative fluoride release in the pairwise comparison ($p < 0.001$).

The values of conventional GICs peak after 24 hours and drop to lower values after 14 days than those of resin-modified GICs. The pattern of fluoride ion release was comparable for all conventional GICs materials. As this additional analysis was conducted with descriptive statistics no statistical tests were performed for this comparison with regard to FO, M and KCE

over time. But pairwise comparison (post hoc Tukey Test in the primary analysis) of conventional and resin-modified glass ionomer cements of the same manufacturer showed a higher cumulative fluoride release from 5 minutes to 6 months in the resin-modified glass ionomer group. Cumulative release was significantly higher when comparing FOLC and FO ($p < 0.001$). MPQM showed higher cumulative fluoride release in comparison to M but the difference was not statistically significant ($p > 0.05$).

Cumulative fluoride ion release, over all measurement times, of all tested materials can be seen in Fig 2.

## Discussion

Many studies have already investigated the fluoride release of both resin-modified glass ionomer cements and conventional glass ionomer cements but show differing results [6, 21, 22].

This might depend on several different conditions regarding the experimental setup. Factors such as the size of the contact surface to test medium [14], the ratio of powder to liquid during the mixing process and the preparation of the coated surface areas [23] should be taken into account, as well as the decisive influence on fluoride release caused by the length of light-curing time on the used GICs [24].

In artificial saliva, fluoride ion release has shown to be lower than in deionized water, because of its higher saturation caused by calcium and phosphate ions [25]. A varying pH value also influences the speed of fluoride release [26]. In solutions with lower pH values, fluoride is released more frequently [27]. To keep the pH value on a persistent level TISAB III with bi-distilled water was used as storage medium in this study. The usage as storage medium is in concordance with other previously published studies [15, 28, 29].

A lot of studies concerning the fluoride release of fluoride varnishes used hydroxyapatite discs as carrying objects [30–32]. Fluoride release is a three-dimensional process in which every surface area will release ions, as long as there is contact with the surrounding solution. In in-vivo situations GICs have a much smaller contact area to saliva due to the bracket and the adhesive gap. Therefore there is a reduced possibility to release fluoride ions than in comparison to GIC covered hydroxyapatite discs in in-vitro procedures.

The use of fluoride free hydroxyapatite discs as carrier for the GICs in this study minimizes the effective fluoride releasing surface and leads to an overall more realistic fluoride release measurement. Human or bovine teeth as a carrier object would bear the risk of possible higher fluoride release due to additional fluoride ion release from the tooth surfaces itself into the surrounding solution [33] and are therefore not suitable for this process.

Fluoride release is also highly dependent on the temperature at which the test samples were stored during the testing period. At 55˚C the fluoride ion release is higher and at 4˚C lower as compared to 37˚C [34–36]. Due to this effect most studies do not use thermocycling and stored the test specimens at a temperature of 37˚C continuously [16, 37, 38]. It has been advocated to use 5–55˚C as a thermocycling process for dental materials in the last twenty years [39] and it has been shown that hot food intake can even achieve higher temperatures [40]. For purposes of scientific standardization this study investigates fluoride concentration dynamics in the surrounding solution at 5–55˚C.

Fluoride release occurs through three mechanisms: washing off the surface, diffusion through the pores and cracks and mass diffusion from deeper layers [36]. A high release is desirable without changing the physical properties or provoking excessive cement degradation [14]. Apart from the influencing factors of the test setup, the filler composition of GICs, solubility of glass particles and reactivity of powder and liquid determine the amount of released fluoride [41, 42]. Particle size also plays an important role. The smaller the filler particles, the

higher is the amount of fluoride released. This is due to an increased surface area created by smaller particles [43].

An increased fluoride release of the resin-modified glass ionomer cements compared to conventional glass ionomer cements might be explained by higher porosity and larger pore size of resin-modified GICs [44–46].

Differences in size of particles or pores of the tested products could explain that a significant difference was found when comparing conventional and resin-modified GIC from the same manufacturer but no statistical significance could be shown in fluoride ion release performance when comparing different manufacturers to each other.

In principle, no general statement can be made by this study as to whether resin-modified or conventional glass ionomer cements release more fluoride as the p-value of Levene's test was 0.3196 (greater than 0.05) the assumption of equality of variances could not be rejected.

Other studies could also not find a clear difference between these two groups [21, 47].

A comparison in the present study of resin-modified and conventional GICs from the same manufacturer showed a higher cumulative fluoride release of resin-modified GICs. A direct comparison is difficult to determine due to different compositions of the products and is not universally transferable. The potential fluoride release of resin-modified GICs is similar to those of conventional GICs, but are affected by several variables. Such as the formation of complex fluoride compounds, the type and quantity of resin used in the photochemical polymerization reaction and their interaction with polyalkenoic acids [48].

The highest amount of fluoride was released within the first 24 hours [21, 34, 49], which is also determined in this study with the highest individual release being achieved at 24 hours across all groups. A reduction in the amount of fluoride ions released can be observed on the second day. This first phase, which can last up to a month, is called the "early or initial burst" phase [50, 51] and could be confirmed by our findings.

After the initial burst which may occur due to loosely bound fluoride [52] a difference in pattern can be seen in conventional and resin-modified glass ionomer cements (28 days, 2 months). It is stated that a stabilization phase of the released fluoride occurs after 7 to 11 days [53]. In this study, the stabilization phase of the released fluoride was found after 2 weeks. The plateau of fluoride release seems higher for resin modified glass ionomer cements (Fig 1). A possible explanation has been described by Cabral et al. stating that the resin components slow down the acid-based reactions and thereby the ionic matrix is able to release more fluoride over time [54]. Interestingly a minimal amount <0.01ppm of fluoride concentration is sufficient to facilitate remineralization in in vitro studies. The minimum concentration in vivo could not be determined [55]. Therefore the differences in plateaus might have clinical relevance.

As the discs were not coated simultaneously at one single time in this study, it can be assumed that there may be minimal differences in the mixing ratio of powder and liquid for the test materials. The measured values of fluoride ion concentration are in a low range that even with the use of a highly sensitive fluoride, as in this study, accuracy cannot be guaranteed. This could also be one of the reasons why a minimal amount of fluoride release was measured in the control group with hydroxyapatite discs. Contamination of the storage solution as possible error could not be ruled out. Other studies have also shown minimal fluoride release from hydroxyapatite discs serving as a control group [54].

This study has an in-vitro character therefore further research should focus on clinical research in order to validate our findings and their effect on the incidence of WSL under clinical conditions.

## Conclusion

All used products released fluoride ions over the entire test period. The highest release was achieved with Fuji Ortho LC (FOLC), the lowest release was achieved with Ketac Cem Easymix (KCE). Comparing the resin-modified and conventional GICs from the same manufacturer (FOLC vs FO by GC Orthodontics and MPQM vs M by VOCO), it could be noted that resin-modified GICs showed a higher cumulative fluoride release rate than conventional GICs. But comparing the performance of conventional GIC to resin-modified GIC of different manufacturers to one another revealed no statistical significance. Therefore a valid statement for higher fluoride release capacity in general for resin-modified GIC can not be supported.

## Supporting information

**S1 File.**
(DOCX)

## Author Contributions

**Conceptualization:** Gholamreza Danesh.

**Data curation:** Sabrina Tulka, Ella A. Naumova.

**Investigation:** Yasemin Dziuk.

**Methodology:** Sachin Chhatwani, Gholamreza Danesh.

**Project administration:** Ella A. Naumova.

**Supervision:** Sachin Chhatwani, Stephan C. Möhlhenrich.

**Validation:** Sachin Chhatwani, Stephan C. Möhlhenrich.

**Visualization:** Sabrina Tulka.

**Writing – original draft:** Yasemin Dziuk, Sachin Chhatwani.

**Writing – review & editing:** Yasemin Dziuk, Sachin Chhatwani, Stephan C. Möhlhenrich, Sabrina Tulka, Ella A. Naumova, Gholamreza Danesh.

## References

1. Knosel M, Vogel Alvarez R, Blanck-Lubarsch M, Helms HJ. Comparison of potential long-term costs for preventive dentistry treatment of post-orthodontic labial versus lingual enamel cavitations and esthetically relevant white-spot lesions: a simulation study with different scenarios. Head & face medicine. 2019; 15(1):22. https://doi.org/10.1186/s13005-019-0204-x PMID: 31399113

2. Chapman JA, Roberts WE, Eckert GJ, Kula KS, Gonzalez-Cabezas C. Risk factors for incidence and severity of white spot lesions during treatment with fixed orthodontic appliances. American journal of orthodontics and dentofacial orthopedics: official publication of the American Association of Orthodontists, its constituent societies, and the American Board of Orthodontics. 2010; 138(2):188–94. https://doi.org/10.1016/j.ajodo.2008.10.019 PMID: 20691360

3. Akin M, Tazcan M, Ileri Z, Basciftci F. Incidence of White Spot Lesion During Fixed Orthodontic Treatment. Turkish Journal of Orthodontics. 2013; 26:98–102.

4. Mortensen D, Gizani S, Salamara O, Sifakakis I, Twetman S. Monitoring regression of post-orthodontic lesions with impedance spectroscopy: a pilot study. European journal of orthodontics. 2018.

5. Heymann GC, Grauer D. A contemporary review of white spot lesions in orthodontics. Journal of esthetic and restorative dentistry: official publication of the American Academy of Esthetic Dentistry [et al]. 2013; 25(2):85–95. https://doi.org/10.1111/jerd.12013 PMID: 23617380

6. Upadhyay S, Rao A, Shenoy R. Comparison of the amount of fluoride release from nanofilled resin modified glass ionomer, conventional and resin modified glass ionomer cements. Journal of dentistry (Tehran, Iran). 2013; 10(2):134–40. PMID: 23724212

7. Francci C, Deaton TG, Arnold RR, Swift EJ Jr., Perdigao J, Bawden JW. Fluoride release from restorative materials and its effects on dentin demineralization. Journal of dental research. 1999; 78 (10):1647–54. https://doi.org/10.1177/00220345990780101001 PMID: 10520970

8. Cosma LL, Suhani RD, Mesaros A, Badea ME. Current treatment modalities of orthodontically induced white spot lesions and their outcome—a literature review. Medicine and pharmacy reports. 2019; 92 (1):25–30. https://doi.org/10.15386/cjmed-1090 PMID: 30957083

9. Artun J, Brobakken BO. Prevalence of carious white spots after orthodontic treatment with multibonded appliances. European journal of orthodontics. 1986; 8(4):229–34. https://doi.org/10.1093/ejo/8.4.229 PMID: 3466795

10. Shimazu K, Ogata K, Karibe H. Evaluation of the caries-preventive effect of three orthodontic band cements in terms of fluoride release, retentiveness, and microleakage. Dental materials journal. 2013; 32(3):376–80. https://doi.org/10.4012/dmj.2012-283 PMID: 23718996

11. Tantbirojn D, Douglas WH, Versluis A. Inhibitive effect of a resin-modified glass ionomer cement on remote enamel artificial caries. Caries research. 1997; 31(4):275–80. https://doi.org/10.1159/000262411 PMID: 9197933

12. Dionysopoulos D. The effect of fluoride-releasing restorative materials on inhibition of secondary caries formation. Fluoride. 2014; 47:258–65.

13. Hatibovic-Kofman S, Koch G. Fluoride release from glass ionomer cement in vivo and in vitro. Swedish dental journal. 1991; 15(6):253–8. PMID: 1817351

14. Mousavinasab SM, Meyers I. Fluoride release by glass ionomer cements, compomer and giomer. Dental research journal. 2009; 6(2):75–81. PMID: 21528035

15. Bahsi E, Sagmak S, Dayi B, Cellik O, Akkus Z. The evaluation of microleakage and fluoride release of different types of glass ionomer cements. Nigerian journal of clinical practice. 2019; 22(7):961–70. https://doi.org/10.4103/njcp.njcp_644_18 PMID: 31293262

16. Basso GR, Della Bona Á, Gobbi DL, Cecchetti D. Fluoride Release from Restorative Materials. Brazilian Dental Journal. 2011; 22:355–8. https://doi.org/10.1590/s0103-64402011000500001 PMID: 22011888

17. Neelakantan P, John S, Anand S, Sureshbabu N, Subbarao C. Fluoride release from a new glass-ionomer cement. Operative dentistry. 2011; 36(1):80–5. https://doi.org/10.2341/10-219-LR PMID: 21488733

18. Morales-Valenzuelaa AA, Scougall-Vilchisb RJ, Lara-Carrilloc E, Garcia-Contrerasd R, Salmeron-Valdese EN, Aguillón-Solf L. Comparison of Fluoride Release in Conventional Glass-Ionomer Cements with a New Mechanical Mixing Cement. Oral Health Prev Dent. 2020; 18:319–24. https://doi.org/10.3290/j.ohpd.a44034 PMID: 32618455

19. Kucukyilmaz E, Savas S, Kavrik F, Yasa B, Botsali M. Fluoride release/recharging ability and bond strength of glass ionomer cements to sound and caries-affected dentin. Nigerian journal of clinical practice. 2017; 20(2):226–34. https://doi.org/10.4103/1119-3077.178917 PMID: 28091442

20. Bell A, Creanor S, Foye R, Saunders W. The effect of saliva on fluoride release by a glass–ionomer filling material. Journal of oral rehabilitation. 1999; 26(5):407–12. https://doi.org/10.1046/j.1365-2842.1999.00389.x PMID: 10373088

21. Cabral MFC, Martinho RLdM, Guedes-Neto MV, Rebelo MAB, Pontes DG, Cohen-Carneiro F. Do conventional glass ionomer cements release more fluoride than resin-modified glass ionomer cements? Restorative dentistry & endodontics. 2015; 40(3):209–15. https://doi.org/10.5395/rde.2015.40.3.209 PMID: 26295024

22. Selimovic-Dragas M, Hasic-Brankovic L, Korac F, Dapo N, Huseinbegovic A, Kobaslija S, et al. In vitro fluoride release from a different kind of conventional and resin modified glass-ionomer cements. Bosnian journal of basic medical sciences. 2013; 13(3):197–202. https://doi.org/10.17305/bjbms.2013.2362 PMID: 23988173

23. McKnight-Hanes C, Whitford GM. Fluoride release from three glass ionomer materials and the effects of varnishing with or without finishing. Caries research. 1992; 26(5):345–50. https://doi.org/10.1159/000261466 PMID: 1468098

24. Ulukapi H, Benderli Y, Soyman M. Determination of fluoride release from light-cured glass-ionomers and a fluoridated composite resin from the viewpoint of curing time. Journal of oral rehabilitation. 1996; 23(3):197–201. https://doi.org/10.1111/j.1365-2842.1996.tb01233.x PMID: 8667126

25. Hattab FN, Amin WM. Fluoride release from glass ionomer restorative materials and the effects of surface coating. Biomaterials. 2001; 22(12):1449–58. https://doi.org/10.1016/s0142-9612(00)00253-2 PMID: 11374443

26. Carey CM, Spencer M, Gove RJ, Eichmiller FC. Fluoride release from a resin-modified glass-ionomer cement in a continuous-flow system. Effect of pH. Journal of dental research. 2003; 82(10):829–32. https://doi.org/10.1177/154405910308201013 PMID: 14514765

**27.** Moreau JL, Xu HHK. Fluoride releasing restorative materials: Effects of pH on mechanical properties and ion release. Dental materials: official publication of the Academy of Dental Materials. 2010; 26(11): e227–e35. https://doi.org/10.1016/j.dental.2010.07.004 PMID: 20708253

**28.** Furtos G, Cosma V, Prejmerean C, Moldovan M, Brie M, Colceriu A, et al. Fluoride release from dental resin composites. Materials Science and Engineering: C. 2005; 25(2):231–6.

**29.** Okte Z, Bayrak S, Fidanci UR, Sel T. Fluoride and aluminum release from restorative materials using ion chromatography. Journal of Applied Oral Science. 2012; 20(1):27–31. https://doi.org/10.1590/s1678-77572012000100006 PMID: 22437674

**30.** Ahmed I, Coleman S, Carey C. Fluoride release and uptake into hydroxyapatite from experimental dental varnish. Journal of dental research. 2013; 92(spec iss A):3259.

**31.** Manarelli MM, Pessan JP, Delbem AC, Amaral JG, Paiva MF, Barbour ME. Protective effect of phosphates and fluoride on the dissolution of hydroxyapatite and their interactions with saliva. Caries research. 2017; 51(2):96–101. https://doi.org/10.1159/000452716 PMID: 28122365

**32.** Kamarudin A, Anderson P, Hill R. The effect of different fluoride varnishes on the release of calcium ions from hydroxyapatite discs: An ion-selective electrodes study. Padjadjaran Journal of Dentistry. 2020; 32(2):82–90.

**33.** Lippert F, Juthani K. Fluoride dose-response of human and bovine enamel artificial caries lesions under pH-cycling conditions. Clinical oral investigations. 2015; 19(8):1947–54. https://doi.org/10.1007/s00784-015-1436-1 PMID: 25731698

**34.** Madhyastha P, Kotian R, Pai V, Khader A. Fluoride Release from Glass Ionomer Cements: Effect of Temperature, Time Interval and Storage Condition2013.

**35.** Yan Z, Sidhu SK, Mahmoud GA, Carrick TE, McCabe JF. Effects of temperature on the fluoride release and recharging ability of glass ionomers. Operative dentistry. 2007; 32(2):138–43. https://doi.org/10.2341/06-36 PMID: 17427822

**36.** Verma S, Loomba K, Tikku A, Chandra A, Verma P, Sharma VP, et al. Comparativ Evaluation of Fluoride and rechargin of glass ionomers under different temperature conditions—an in-vitro study2015. 9–14 p.

**37.** Bansal R, Bansal T. A Comparative Evaluation of the Amount of Fluoride Release and Re-Release after Recharging from Aesthetic Restorative Materials: An in vitro Study. J Clin Diagn Res. 2015; 9(8): ZC11–ZC4. https://doi.org/10.7860/JCDR/2015/11926.6278 PMID: 26436037

**38.** Brzović-Rajić V, Miletić I, Gurgan S, Peroš K, Verzak Ž, Ivanišević-Malčić A. Fluoride Release from Glass Ionomer with Nano Filled Coat and Varnish. Acta Stomatol Croat. 2018; 52(4):307–13. https://doi.org/10.15644/asc52/4/4 PMID: 30666061

**39.** Morresi AL, D'Amario M, Capogreco M, Gatto R, Marzo G, D'Arcangelo C, et al. Thermal cycling for restorative materials: does a standardized protocol exist in laboratory testing? A literature review. Journal of the mechanical behavior of biomedical materials. 2014; 29:295–308. https://doi.org/10.1016/j.jmbbm.2013.09.013 PMID: 24135128

**40.** Youngson C, Barclay C. A pilot study of intraoral temperature changes. Clinical oral investigations. 2000; 4(3):183–9. https://doi.org/10.1007/s007840000060 PMID: 11000326

**41.** Shiozawa M, Takahashi H, Iwasaki N. Fluoride release and mechanical properties after 1-year water storage of recent restorative glass ionomer cements. Clinical oral investigations. 2014; 18(4):1053–60. https://doi.org/10.1007/s00784-013-1074-4 PMID: 23974799

**42.** Xu X, Burgess JO. Compressive strength, fluoride release and recharge of fluoride-releasing materials. Biomaterials. 2003; 24(14):2451–61. https://doi.org/10.1016/s0142-9612(02)00638-5 PMID: 12695072

**43.** Mungara J, Philip J, Joseph E, Rajendran S, Elangovan A, Selvaraju G. Comparative evaluation of fluoride release and recharge of pre-reacted glass ionomer composite and nano-ionomeric glass ionomer with daily fluoride exposure: an in vitro study. Journal of the Indian Society of Pedodontics and Preventive Dentistry. 2013; 31(4):234–9. https://doi.org/10.4103/0970-4388.121820 PMID: 24262396

**44.** Dionysopoulos P, Kotsanos N, Pataridou A. Fluoride release and uptake by four new fluoride releasing restorative materials. Journal of oral rehabilitation. 2003; 30(9):866–72. https://doi.org/10.1046/j.1365-2842.2003.00993.x PMID: 12950966

**45.** Hsu HM, Huang GF, Chang HH, Wang YL, Guo MK. A continuous flow system for assessing fluoride release/uptake of fluoride-containing restorative materials. Dental materials: official publication of the Academy of Dental Materials. 2004; 20(8):740–9. https://doi.org/10.1016/j.dental.2003.10.008 PMID: 15302455

**46.** Okte Z, Bayrak S, Fidanci UR, Sel T. Fluoride and aluminum release from restorative materials using ion chromatography. Journal of applied oral science: revista FOB. 2012; 20(1):27–31. https://doi.org/10.1590/s1678-77572012000100006 PMID: 22437674

**47.** Gao W, Smales RJ. Fluoride release/uptake of conventional and resin-modified glass ionomers, and compomers. Journal of dentistry. 2001; 29(4):301–6. https://doi.org/10.1016/s0300-5712(00)00053-1 PMID: 11525231

**48.** Kucukyilmaz E, Savas S, Kavrik F, Yasa B, Botsali MS. Fluoride release/recharging ability and bond strength of glass ionomer cements to sound and caries-affected dentin. Nigerian journal of clinical practice. 2017; 20(2):226–34. https://doi.org/10.4103/1119-3077.178917 PMID: 28091442

**49.** Chan WD, Yang L, Wan W, Rizkalla AS. Fluoride release from dental cements and composites: a mechanistic study. Dental materials: official publication of the Academy of Dental Materials. 2006; 22 (4):366–73. https://doi.org/10.1016/j.dental.2005.04.028 PMID: 16087226

**50.** Nagi SM, Moharam LM, El Hoshy AZ. Fluoride release and recharge of enhanced resin modified glass ionomer at different time intervals. Future Dental Journal. 2018; 4(2):221–4.

**51.** Sidhu SK, Nicholson JW. A Review of Glass-Ionomer Cements for Clinical Dentistry. Journal of functional biomaterials. 2016; 7(3):16. https://doi.org/10.3390/jfb7030016 PMID: 27367737

**52.** Verbeeck RM, De Maeyer EA, Marks LA, De Moor RJ, De Witte A, Trimpeneers LM. Fluoride release process of (resin-modified) glass-ionomer cements versus (polyacid-modified) composite resins. Biomaterials. 1998; 19(6):509–19. https://doi.org/10.1016/s0142-9612(97)00131-2 PMID: 9645557

**53.** Can-Karabulut DC, Batmaz I, Solak H, Tastekin M. Linear regression modeling to compare fluoride release profiles of various restorative materials. Dental materials: official publication of the Academy of Dental Materials. 2007; 23(9):1057–65. https://doi.org/10.1016/j.dental.2006.06.046 PMID: 17161861

**54.** Chau NPT, Pandit S, Jung J-E, Jeon J-G. Evaluation of Streptococcus mutans adhesion to fluoride varnishes and subsequent change in biofilm accumulation and acidogenicity. Journal of dentistry. 2014; 42 (6):726–34. https://doi.org/10.1016/j.jdent.2014.03.009 PMID: 24694978

**55.** Hellwig E, Lussi A. What is the optimum fluoride concentration needed for the remineralization process? Caries research. 2001; 35 Suppl 1:57–9. https://doi.org/10.1159/000049112 PMID: 11359060