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# BIOMIMETIC MINERALIZATION APPROACH OF DENTIN HYPERSENSITIVITY IN PATIENTS WITH EARLY NON-CARIOUS CERVICAL LESIONS

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## *ABSTRACT*

**Objective:** to evaluate the efficacy of non-invasive procedures through biomimetic mineralization of a fluoride, bioactive glass with and without fluoride and self-organizing peptides in the treatment of dentinal hypersensitivity due to early non-carious cervical lesions.

**Materials and methods:** Twenty-eight patients with self-reported history of dentin hypersensitivity were evaluated sequentially for evidence of erosion, abrasion or gingival recession at facial cervical region. Patients were randomly distributed into four treatment groups of seven patients each according to the type of the treatment (group I: Elmex Gele'e, group II: BioMin™ F, group III: BioMin™ C group IV: Curodont™ D'senz). The teeth were subjected to five follow up periods (baseline, after 3,6,9 and 12 weeks) and assessed in response to evaporative air-blast stimulus utilizing Schiff Sensitivity Scale and Visual Analogue Scale. Electrical test was performed utilizing electrical pulp tester. The extent of tubule occlusion was examined under scanning electron microscope using negative replica of randomly selected patients.

**Results:** All the tested groups showed different degrees of relieving dentinal hypersensitivity symptoms with significant difference throughout the different assessment periods. The difference between the studied groups was statistically significant. Under SEM, group II, III and IV showed complete tubule occlusion. However, group I showed partial tubule occlusion.

**Conclusions:** Elmex® gelée, BioMin™ F, BioMin™ C and Curodont™ D'senz were effective to manage dentin hypersensitivity related to early non-carious cervical lesions based on the biomimetic mineralization concept that has focused on permanent management of dentin hypersensitivity.

**KEYWORDS:** Fluoride, Bioactive glass, self-organizing peptides, non-carious cervical lesions, dentin hypersensitivity.

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## INTRODUCTION

Dentin hypersensitivity (DH) is a commonly encountered clinical condition causing significant physical and psychological discomfort that can have a significant impact on oral health and functioning[1] as patients are unable to maintain proper oral hygiene and perform adequate plaque control measures in hypersensitive areas thus leading to further plaque accumulation and degradation in gingival or periodontal health [2].

Physiological and morphological studies have shown that, dentin hypersensitivity in non-carious cervical lesions (NCCLs) occurs when the dentinal tubules are exposed to the oral environment as a consequence of enamel loss and/or [3] cementum loss due to gingival recession or tooth wear process involving attrition, abrasion and/or erosion [4].

Dentin hypersensitivity is based on a diagnosis of exclusion. The clinician should use all his skills in gaining the necessary information relating to a patient's history, screening and identification of etiologic and predisposing factors, particularly dietary and oral hygiene habits. This is in order to make a definite diagnosis [5].

Several mechanisms of action were described to explain dentin hypersensitivity. The most accepted mechanism is based on the hydrodynamic theory proposed by Brännström which suggested that, pain results of rapid fluid movement in the dentinal tubules due to external stimuli, typically thermal, tactile, evaporative, osmotic, and chemical triggers. Stimulus-induced fluid flow might activate nerve endings, (A-β and A-δ fibers) at the dentin-pulp interface leading to the pain response [6].

The management of dentin hypersensitivity should be based on a stepwise approach controlled by the extent and severity of the condition. Clinically, there are many treatment modalities that provide relief of dentin hypersensitivity. Generally, this might be achieved via one of two different modes of action: (i) direct diffusion of depolarizing agents, such as potassium ions, to reduce intra-dental nerve activity by sustained depolarization and axonal accommodation, making the nerve less excitable to further stimulation and (ii) physical blockage of the open dentinal tubules with occluding agents [4].

Current research focuses on increasing the mineral density of the dentin surface making it possible to improve its resistance to wear by both acid erosion and abrasion and plugging and sealing open tubules with a calcium and phosphate containing dentin-like substance, which would block diffusion through the tubules into the dentin sub-surface, thereby increasing acid resistance [4,7].

The ideal treatment for dentin hypersensitivity should be effective, long term, cheap, and simple to use. Toothpastes, mouthwashes, and gels are the most commonly used agents, as they are noninvasive and have a favorable cost–benefit ratio [8].

Intensive topical fluoridation using (Elmex® gelée) will help in remineralization and can relieve dentinal hypersensitivity through effective closing exposed dentinal tubules[9]. Recently, calcium phosphosilicate, patented bioactive glass toothpaste (BioMin®) is designed and optimized as a desensitizing toothpaste that contains calcium, phosphate, and silica. Upon contact with aqueous environment, it forms apatite that occludes the dentinal tubules, promotes remineralization and help reduce tooth sensitivity. BioMin™ F releases fluoride in addition to calcium and phosphate that released from BioMin™ C [10]. On the other hand, the first preself-assembled peptide product (Curodont D'Senz®) for dentin hypersensitivity has been launched and reported to form stable and highly effective protective barrier on the tooth surface [11].

It was reported that, the reproducibility of assessment methods of DH was hard to achieve, even if standardized techniques were used. Hence it was recommended that the outcome evaluation of DH treatment in clinical practice as well as in clinical trials should comprise at least two different stimuli, and to use both assessment methods which are stimulus- and response-based assessments [5].

Replica techniques, utilizing rubber base impression of the affected teeth together with scanning electron microscopy (SEM) imaging, have been used to gain an inverse image of the tooth surface, facilitating visualization of the agglutinated or enlarged dentinal tubules in areas of DH and provided valuable information [12].

There are deficient clinical studies that evaluate the effectiveness of biomimetic mineralization in treatment of human dentinal hypersensitivity. So, the aim of the present study is to evaluate the efficacy of biomimetic mineralization by using fluoride, bioactive glasses and preself-assembled peptides in the treatment of dentinal hypersensitivity due to loss of cervical enamel surface.

## MATERIALS AND METHODS

Twenty-eight patients with an age ranging between (20–45 years) with self-reported history of dentin hypersensitivity were selected to participate in the present study. They were randomly distributed into four treatment groups of seven patients each. Materials, compositions, and manufacturers are summarized in Table-1.

### Screening and Selection Procedures

At the screening visit; all the participants were subjected to oral examination, in addition to medical and social history review. To determine eligibility, each participant's dentition was evaluated sequentially for evidence of erosion, abrasion or

TABLE (1) Materials used in the present study.

| Materials | Chemical compositions | Manufacturer | Web site |
|---|---|---|---|
| **Elmex® gelée Fluoride gel** | 100 g of dental gel containing active ingredients:<br>• diidrofluoruro of bis (hydroxyethyl) amino-propyl-N-hydroxyethyl-octadecylamine 3,032 g<br>• hydrofluoride of octadecylamine 0.287 g<br>• Sodium fluoride 2,210 (total fluorine content = 1.25%)<br>Excipients: Propylene glycol, hydroxyethyl cellulose, saccharin, spearmint oil, peppermint oil, banana flavor, apple flavor, DL-menthone, purified water | CP GABA GmbH | http://www.elmex.ch |
| **BioMin™ F Toothpaste** | Glycerin, Silica, PEG 400, Fluoro CalciumPhosphoSilicate, Sodium Lauryl Sulphate, Titanium Dioxide, Aroma, Carbomer, Potassium Acesulfame.<br>Available Fluoride content <600ppm when packed | BioMin Technologies Limited, London | Email: info@biomin.co.uk http://www.biomin.co.uk/ |
| **BioMin™ C Toothpaste** | Glycerin, Silica, PEG, Sodium Lauryl Sulphate, ChloroCalciumPhosphoSilicate, Titanium Dioxide, Flavouring, Carbopol, Potassium Acesulfame. | BioMin Technologies Limited, London | |
| **Curodont™ D'senz gel** | Self-organizing biomimetic molecules/peptides. peptide (P11-4) (preself-assembled particles) based on the clinically tested and award-winning CUROLOX® Technology | Credentis ag swiss. | www.curodont.com /en/curodont-dsenz/. |
| **Aquasil Ultra LV Impression material** | Polydimethylsiloxane polymer; Polymethylhydrogen Siloxane; Silicon Dioxide; Sodium Aluminosilicate; Organic Platinum Complex; Surfactant; Titanium Dioxide; Metallic Oxide Pigments; Peppermint Oil. | Dentsply Caulk, USA | www.dentsplysirona.com |

gingival recession (EAR) at cervical region of facial surfaces and sensitivity response to an evaporative air-blast stimulus (as indicated by a 'yes' response when the subject was questioned about discomfort following stimulation). From those teeth that had a Schiff Sensitivity Score ≥2 [13] and an occlusion score of 4–5 [12] as determined by scanning electron microscope of replica impressions of the sensitive area, the investigator selected 'test teeth' for each eligible patient to be assessed for the remainder of the study [14].

All selected patients received a scaling and polishing procedure before the study and instructed to cease other desensitizing agents, such as desensitizing toothpastes and mouth rinses prior to and through the duration of the study [15].

**Treatment approaches**

At the baseline visit, patients were assessed for continuing eligibility. Sensitivity of eligible teeth identified at screening was evaluated so that, the tooth selected at baseline had to demonstrate the same minimum Schiff Sensitivity and occlusion scores as required for eligibility at the screening visit for progression into the treatment phase.

Eligible patients were randomly distributed into four treatment groups of seven patients each (1:1:1:1) as follows:

- **Group I**: Received Elmex Gele'e fluoride gel
- **Group II**: Received BioMin™ F toothpaste.
- **Group III**: Received BioMin™ C toothpaste.
- **Group IV**: Received Curodont™ D'senz gel.

Concerning groups II and III, study toothpastes BioMin™ F and BioMin™ C respectively were applied with a manual toothbrush Oral-B (Procter & Gamble USA) by applying one-centimeter-long bead of toothpaste to the toothbrush provided. Patients were instructed to brush with their recommended study toothpaste for one minute twice daily twelve hours apart (morning and evening). After one minute of brushing, the toothpaste was swirled around the mouth for thirty seconds, and spitted out the excess into the sink. No rinsing was permitted [10].

Regarding group I, Elmex Gele'e flouride gel; Brushing was done once a week by application of one centimeter of gel to toothbrush provided followed by spitting out and rinsing it off after two to three minutes [9]. As recommended by manufacturer's instructions. While application of Curodont ™ D'senz in group IV was done by either method following manufacturer's instructions by applying Curodont ™ D'senz gel with a rubber polisher or with rubbing finger directly onto the sensitive area of tooth surface [11].

To facilitate compliance, the patient's first brushing was carried out under supervision at the baseline visit. Further supervised brushings were carried out at the end of the 3, 6, 9 and 12 week visits. Compliance with toothpaste usage instructions was assessed by visual inspection of the returned toothpaste tubes. During the study, patients were controlled, advised and not permitted to use any oral care products or any dental products (including home remedies) other than those provided intended for treating sensitive teeth [14].

**Assessment of cervical dentin hypersensitivity**

The selected sensitive teeth were evaluated at baseline immediately after application, after 3,6,9 and 12 weeks using the two stimuli; evaporative air-blast and electrical stimuli. The stimuli tests were applied with a five minutes' pause between the applications of different stimuli [14].

Dentin hypersensitivity assessments were performed and recorded by the same examiner following the same methodology employed at the baseline examination and for all assessments throughout the duration of the study [16].

**Evaporative air-blast sensitivity stimulus**

These assessments were performed by directing a three seconds of compressed air from a triple air

dental syringe at 60 psi (±5 psi) onto the affected area of the tooth in a distance of approximately one centimeter away from the cervical region of the teeth while the adjacent teeth were isolated using cotton rolls [17].

Two response measures were undertaken, an examiner-based Schiff Sensitivity Scale (SSS) assessment and a subjective assessment utilizing a Visual Analogue Scale (VAS) [14].

**Examiner assessment using Schiff Sensitivity Scale (SSS):**

Based on the following Schiff Sensitivity Scale; the higher the score, the higher the level of dentin hypersensitivity [13].

- **Score 0:** Subject does not respond to stimulus (no significant discomfort or awareness of stimulus).
- **Score 1:** Subject responds to stimulus but does not request discontinuation of stimulus (discomfort but no severe pain).
- **Score 2:** Subject responds to stimulus and requests discontinuation or moves from stimulus (pain during application of stimulus).
- **Score 3:** Subject responds to stimulus, considers stimulus to be painful, and requests discontinuation of the stimulus (severe pain during and after application of stimulus).

**Subjective assessment using Visual analogue scale (VAS)**

Patients were asked to place a mark on a 100 millimeter (10 centimeter) line that represented their level of perceived pain intensity that indicate the intensity of the sensitivity or discomfort caused by the stimulus. The distance of this mark in millimeters from the left end of the scale was recorded and used as the VAS score [18]. These data with stipulated ratings ranging as from:

- **Score 0:** no pain
- **Score up to 2cm:** mild pain
- **Score 2-4 cm** moderate pain
- **Score 4-6 cm:** severe pain.
- **Score 6-8 cm:** very severe pain.
- **Score 8-10 cm:** worst pain possible.

**Electrical sensitivity assessment**

The electrical pulp testing using Digitest ™ II* was performed to measure facial cervical third site and was used to check the numerical value, and when the value was higher than the previous visit, the dentin hypersensitivity was mitigated. The numbers appearing on the device are meaningless, and they are meaningful for the range of change of the numerical value (5→10, 10→15). When the patient felt a higher electric resistance at each consecutive visit, the answer was judged that there was a notable dentin hypersensitivity relieving effect and there was a noted effect of the toothpaste or gel used [19].

**Negative replica and scanning electron microscope (SEM) analysis for tubular occlusion assessment**

An impression of some randomly selected hypersensitive area of the selected teeth was performed and analyzed using scanning electron microscope. Throughout the study, negative replica was obtained immediately following the clinical sensitivity assessment. Prior to obtaining the replica impression, the surface of the selected tooth was wiped using a sterile damp cotton wool roll, with care taken to ensure no cotton was left on the tooth surface then the impression was taken immediately. The silicone based impression material Aquasil Ultra LV®* was applied directly to the tooth surface

* Digital Electerical Pulp Vitality Tester, parkell, USA).

and held in place for five minutes as instructed by the manufacturer.

Then replica impression of the sensitive area was analyzed directly via scanning electron microscope** without the need to cast a further positive replica to investigate the degree of dentin tubule occlusion. Using the gingival margin as a reference to ensure that approximately the same location of the replica impression of the tooth was examined on each occasion.

The images were taken at fixed magnification of ×500 then the extent of tubule occlusion was assessed and scored according to 5-point categorical scale in accordance with the ranking system established below that visualize the extent of occlusion (visual score) [12].

- **Score 0**: Not evaluable.
- **Score 1**: Occluded (100% of tubules occluded).
- **Score 2**: Mostly occluded (75% of tubules occluded).
- **Score 3**: Equally occluded/un-occluded (50% of tubules occluded).
- **Score 4**: Mostly un-occluded (25% of tubules occluded).
- **Score 5**: Un-occluded (0%: no tubule occlusion).

Percentage of tubule occlusion (% OCT) was evaluated using the formula:

% OCT= (Number of occluded tubules × 100) ÷ Total number of Tubules.

*[Dentsply Caulk, USA].

**JEOL - JSM-6510LV, Scanning Electron Microscope, Japan.

**Statistical analysis:**

The collected data monitoring the behavior of each tested material by all measures along the different evaluation periods were tabulated and statistically analyzed so that, numerical variables are expressed by descriptive statistics as mean, standard deviation and range. Repeated measures ANOVA was used to compare durations within group, one-way ANOVA and post hock test (Tukey-test) were used to comparing groups in the same duration. Nonparametric variables are expressed as mean and median. Freidman test was used to compare durations within group, Kurskal-Wallis H, Mann Whitney U test were used to comparing groups in the same duration. P-value <0.05(*) was considered significant difference & P-value <0.001(**) was considered highly significant difference. Statistical analyses were performed using Statistical Package for Social Sciences (SPSS version 26).

## RESULTS

### Examiner assessment Schiff Sensitivity Scale (SSS)

Friedman's test was used to compare the mean and median Schiff Sensitivity score values from baseline to successive follow-up periods within each tested group. As shown in Table-2. A high statistically significant difference (P=0.000) was recorded within each group throughout the different assessment periods.

### Visual analogue scale (VAS)

Mean and median values of Visual analogue scores of pain intensity for evaporative air-blast stimulus for different interventions and follow-up intervals are presented in Table-3. As shown, the results for statistical analysis within each study group comparing different evaluation times revealed a high statistically significant (P < 0.000) decrease in pain intensity based on mean VAS score values before and after treatment that was noted in each study group through successive follow-up intervals indicating that all study groups recorded a significant improvement in dentin hypersensitivity symptoms from baseline to twelve weeks.

Inter group comparison of VAS score mean values were performed using Kruskal Wallis test as shown in Table-3. The longitudinal changes for the VAS score mean values were significantly different among all tested groups at 3 ,6 and 9 weeks (p= 0.013, 0.012 and 0.024 respectively). Thus, pair-wise Mann-Whitney test was performed to detect the statistical difference between each two groups as shown in Tables-4:6. The significant difference was found between group III versus group I and group II at 3 weeks (P= of 0.007 and 0.017 respectively) and at 6 weeks (P= of 0.026 and 0.004 respectively) indicating that patients treated with BioMin™ C showed significantly highest pain relief compared to those treated with Elmex Gele'e and BioMin™ F at such assessment periods. While, at 6 weeks there was a significant difference between group III versus group IV (p=0.026) denoting that patients treated with BioMin™ C exhibited significant more dentinal hypersensitivity reduction compared to those treated with Curodont ™ D'senz at 6 weeks. In addition, there was a statistically significant difference between group IV versus group I and III at 9 weeks recording p value of 0.025, 0.025 respectively indicating that patients treated with Curodont ™ D'senz had lowest pain relief in comparison with those treated with Elmex Gele'e and BioMin™ C at 9 weeks.

TABLE (2): Statistical analysis of the Mean and Median values of Schiff Sensitivity scores of all groups through the different assessment periods.

| Assessment periods / Groups | Baseline | 3 Weeks | 6 Weeks | 9 Weeks | 12 Weeks | Friedman's test | p-value |
|---|---|---|---|---|---|---|---|
| | Mean (M) | Mean (M) | Mean (M) | Mean (M) | Mean (M) | | |
| **Group I** | 2.14(2) | 1.86(1) | 0.57(0) | 0(0) | 0(0) | 26.017 | 0.000** |
| **Group II** | 2.14(2) | 2.14(2) | 0.71(1) | 0.29(0) | 0.14(0) | 23.311 | 0.000** |
| **Group III** | 2.29(2) | 0.29(0) | 0(0) | 0(0) | 0(0) | 25.073 | 0.000** |
| **Group IV** | 2.29(2) | 0.71(0) | 0.29(0) | 0.29(0) | 0(0) | 20.277 | 0.000** |
| **Kurskal-Wallis test** | 0.0001 | 0.464 | 0.082 | 2.167 | 1.000 | ---------- | |
| **p-value** | 1.000 | 0.496 | 0.775 | 0.141 | 0.317 | ---------- | |

***There is a significant at P-value< 0.05 (*), and highly significant at P-value< 0.001 (**).***

TABLE (3): Statistical analysis of the Mean and Median values of Visual Analogue scores of all groups through the different assessment periods.

| Assessment periods / Groups | Baseline | 3 Weeks | 6 Weeks | 9 Weeks | 12 Weeks | Friedman's test | p-value |
|---|---|---|---|---|---|---|---|
| | Mean (M) | Mean (M) | Mean (M) | Mean (M) | Mean (M) | | |
| **Group I** | 6.43(6) | 4.43(6) | 2.3(2) | 0(0) | 0.071(0) | 25.240 | 0.000** |
| **Group II** | 4.71(5) | 4.14(4) | 2.71(4) | 1(0) | 0.286(0) | 22.624 | 0.000** |
| **Group III** | 6(7) | 1.29(1) | 0(0) | 0(0) | 0.071(0) | 24.289 | 0.000** |
| **Group IV** | 4.14(4) | 2.43(2) | 1.29(1) | 1.86(2) | 0(0) | 19.344 | 0.001** |
| **Kurskal-Wallis H** | 5.300 | 10.843 | 11.034 | 9.443 | 1.088 | ---------- | |
| **p-value** | 0.151 | 0.013* | 0.012* | 0.024* | 0.780 | ---------- | |

***M-> median.***

TABLE (4): Intergroup statistical comparison between all groups at second evaluation period (3 weeks).

| Mann-Whitney Test | Group I | Group II | Group III | Group IV |
|---|---|---|---|---|
| **Group I** | - | 0.710 | 0.007* | 0.128 |
| **Group II** | 0.710 | - | 0.017* | 0.073 |
| **Group III** | 0.007* | 0.017* | - | 0.128 |
| **Group IV** | 0.128 | 0.073 | 0.128 | - |

TABLE (5): Intergroup statistical comparison between all groups at third evaluation period (6 weeks).

| Mann-Whitney Test | Group I | Group II | Group III | Group IV |
|---|---|---|---|---|
| **Group I** | - | 0.805 | 0.026* | 0.456 |
| **Group II** | 0.805 | - | 0.004* | 0.209 |
| **Group III** | 0.026* | 0.004* | - | 0.026* |
| **Group IV** | 0.456 | 0.073 | 0.209 | - |

TABLE (6): Intergroup statistical comparison between all groups at fourth evaluation period (9 weeks).

| Mann-Whitney Test | Group I | Group II | Group III | Group IV |
|---|---|---|---|---|
| **Group I** | - | 0.062 | 1.000 | 0.025* |
| **Group II** | 0.062 | - | 0.062 | 0.410 |
| **Group III** | 1.000 | 0.062 | - | 0.025* |
| **Group IV** | 0.025* | 0.410 | 0.025* | - |

**Electrical sensitivity assessment result**

The means and standard deviations values of electrical sensitivity test for different treatments and follow-up assessment periods throughout the study time are presented as a descriptive analysis in Table-7. As shown, dentin hypersensitivity relaxation effect was observed as a continuous progression of dentin hypersensitivity mitigation in all groups manifested by the gradual increase in the recorded mean values in the different follow up periods. Therefore, Testing the effect of time within each study group, a statistically significant reduction in dentin hypersensitivity levels from baseline to each all-subsequent follow-up periods was represented by p values of 0.007, 0.042, 0.002 and 0.001 in groups I, II, III and IV respectively.

Comparing the four study groups at each assessment period, One-way ANOVA test revealed a statistically significant difference at baseline and 3 weeks (P= 0.004 and P= 0.018 respectively) and a highly statistically significant difference (P=0.000) at 12 weeks as shown in Table-7. Thus, pair-wise post hock test (Tukey's test) was performed to detect the statistical difference between each two groups as shown in Tables-8:10.

The significant difference was found between group I versus group II at baseline (P= of 0.002) indicating that group I (7.29) exhibited higher sensitivity than group II (16.86). In addition, group I versus groups II and III at 3 weeks (P= of 0.033 and 0.024 respectively) revealing that the recorded mean value (9.43) in group I still lower than both groups II and III (17.71and 18.14 respectively) and denoting that it was still exhibiting higher sensitivity than both groups with little effect of treatment on dentin hypersensitivity. While, at 12 weeks, group IV recorded significant difference versus group I and group II (P= of 0.002 and 0.002 respectively) and highly significant difference from group III (P=0.000) revealing that group IV recorded the highest mean value (46.43) as compared to group I, II and III (27.86 and 28 and 23.86 respectively) and demonstrated with the highest dentin hypersensitivity relief effect.

**Negative replica and scanning electron microscope analysis for tubular occlusion assessment.**

As presented in Table-11, Friedman's test revealed a statistically significant difference within

TABLE (7): Descriptive statistics showing the mean and standard deviation values of electrical sensitivity test of all study groups through the different evaluation periods.

| Assessment periods / Groups | Baseline Mean±SD | 3 weeks Mean±SD | 6 weeks Mean±SD | 9 weeks Mean±SD | 12 weeks Mean±SD | F | p-value |
|---|---|---|---|---|---|---|---|
| **Group I** | 7.29±5.02 | 9.43±3.82 | 16.57±6.48 | 18.86±7.56 | 27.86±9.12 | 9.423 | 0.007* |
| **Group II** | 16.86±4.14 | 17.71±6.10 | 18.14±2.55 | 26±10.77 | 28±12.70 | 3.835 | 0.042* |
| **Group III** | 12.14±4.63 | 18.14±4.26 | 24.14±4.95 | 36.29±11.43 | 23.86±4.95 | 20.943 | 0.002* |
| **Group IV** | 12.86±3.24 | 15.71±6.37 | 27.14±13.37 | 28.43±14.06 | 46.43±3.78 | 17.771 | 0.001* |
| **F** | 5.807 | 4.098 | 2.758 | 2.885 | 10.109 | ---------- | |
| **p-value** | 0.004* | 0.018* | 0.064 | 0.057 | 0.000** | ---------- | |

each group throughout the study assessment periods as occlusion score mean values fell markedly from baseline to subsequent follow ups. This finding indicated that, there was gradual increase in tubule occlusion in groups I, II, III and IV with p values of 0.036, 0.034, 0.021 and 0.001 respectively.

From scanning electron microscopy analysis, it can be observed that, all treatments provided an increase in tubule occlusion throughout the assessment periods ranging from partial tubule occlusion (75% of tubules occluded) in group I as shown in Figure-1-a:e to superior tubule occlusion (100% of tubules occluded) in group II as presented in Figure-2-a:e, group III in Figure-3-a:e and group IV in Figure-4-a:e respectively.

TABLE (8): Intergroup statistical intergroup statistical comparison between all groups at baseline.

| One-way ANOVA. | Group I | Group II | Group III | Group IV |
|---|---|---|---|---|
| **Group I** | - | 0.002* | 0.179 | 0.101 |
| **Group II** | 0.002* | - | 0.200 | 0.328 |
| **Group III** | 0.179 | 0.200 | - | 0.989 |
| **Group IV** | 0.101 | 0.328 | 0.989 | - |

TABLE (9): Intergroup statistical comparison between all groups at second evaluation period (3 weeks).

| One-way ANOVA. | Group I | Group II | Group III | Group IV |
|---|---|---|---|---|
| **Group I** | - | 0.033* | 0.024* | 0.142 |
| **Group II** | 0.033* | - | 0.999 | 0.891 |
| **Group III** | 0.024* | 0.999 | - | 0.823 |
| **Group IV** | 0.142 | 0.891 | 0.823 | - |

TABLE (10): Intergroup statistical comparison between all groups at fifth evaluation period (12 weeks).

| One-way ANOVA. | Group I | Group II | Group III | Group IV |
|---|---|---|---|---|
| **Group I** | - | 1.000 | 0.810 | 0.002* |
| **Group II** | 1.000 | - | 0.794 | 0.002* |
| **Group III** | 0.810 | 0.794 | - | 0.000** |
| **Group IV** | 0.002* | 0.002* | 0.000** | - |

TABLE (11): Statistical analysis of the Mean and Median values of occlusion scores of all groups through the different assessment periods.

| Assessment periods / Groups | Baseline | 3 Weeks | 6 Weeks | 9 Weeks | 12 Weeks | Friedman's test | p-value |
|---|---|---|---|---|---|---|---|
| | Mean (M) | Mean (M) | Mean (M) | Mean (M) | Mean (M) | | |
| **Group I** | 3.67(4) | 3.67(4) | 2.33(2) | 2(2) | 1.67(2) | 10.250 | 0.036* |
| **Group II** | 4.3(5) | 2(2) | 1.67(2) | 1.67(2) | 1(1) | 10.400 | 0.034* |
| **Group III** | 4.67(5) | 3(3) | 1.3(1) | 1(1) | 1(1) | 11.529 | 0.021* |
| **Group IV** | 3.67(4) | 1.67(2) | 1(1) | 2(1) | 1(1) | 17.532 | 0.001* |
| **Kurskal-Wallis H** | 2.588 | 6.523 | 6.587 | 4.492 | 6.600 | ---------- | |
| **p-value** | 0.460 | 0.089 | 0.086 | 0.213 | 0.086 | ---------- | |

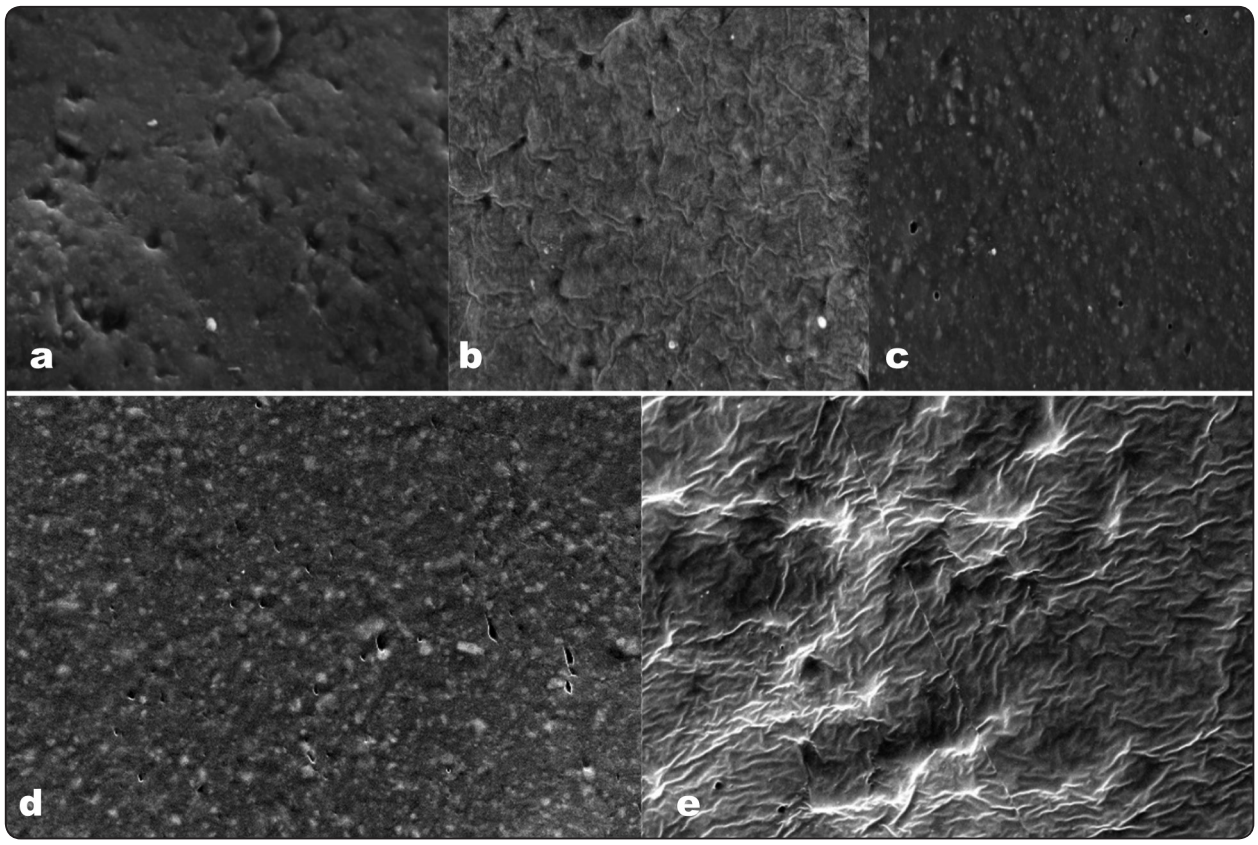


Fig. (1): a) and b) Scanning electron microscopy (SEM) micrographs at magnification ×500 of inverse replica performed on hypersensitive areas of patients treated with Elmex Gele'e (group I) displaying occlusion score 4 where mostly of tubules unoccluded (25% of tubules occluded) at baseline and 3 weeks respectively c), d) and e) occlusion score decreased to 2 where mostly of tubules occluded (75% of tubules occluded) at 6, 9 and 12 weeks respectively.

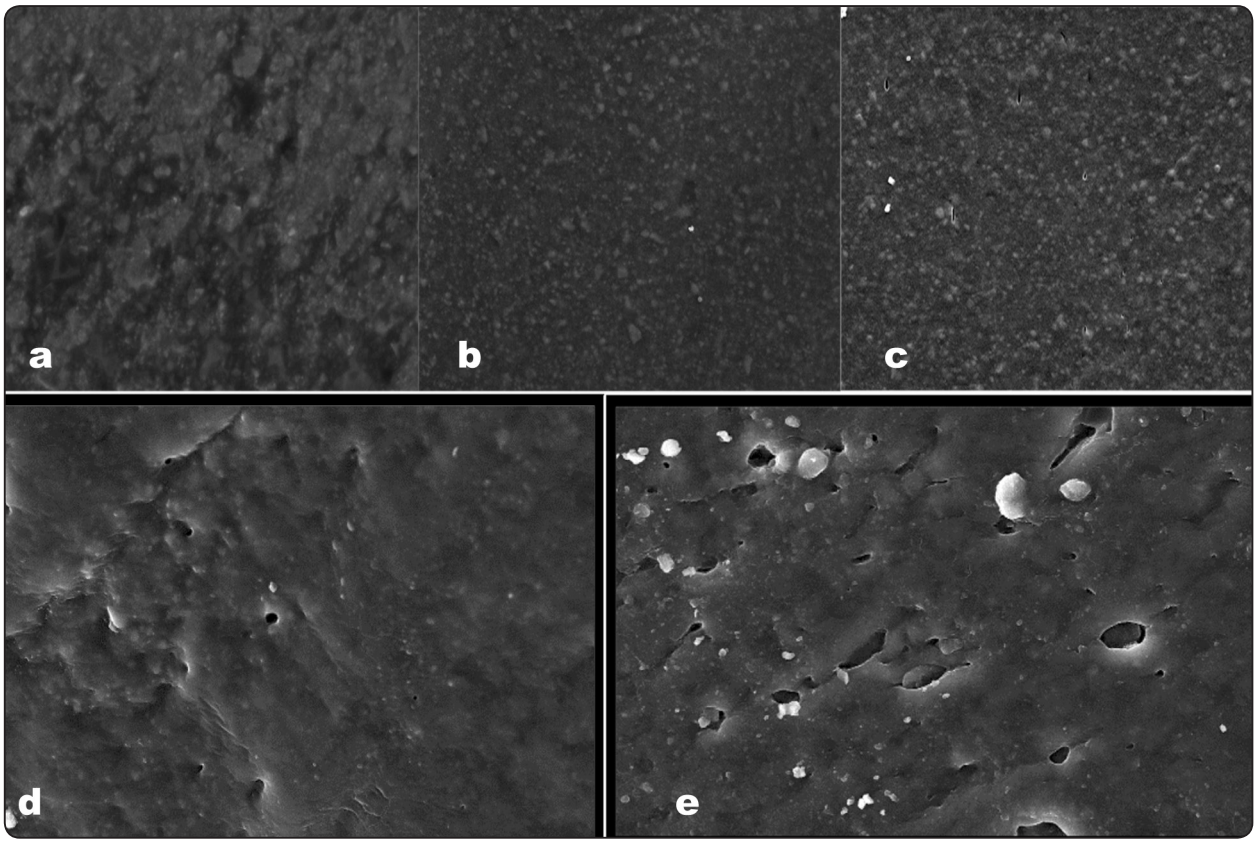


Fig. (2): a) Scanning electron microscopy (SEM) micrographs at magnification ×500 of inverse replica performed on hypersensitive areas of patients treated with BioMin TM F (group II) displaying occlusion score 5 (0%: no tubule occlusion) at baseline. b) occlusion score 3 where there were equally occluded/unoccluded tubules (50% of tubules occluded) at 3 weeks. c) and d) occlusion score decreased to 2 where mostly of tubules occluded (75% of tubules occluded) at 6 and 9 weeks respectively. e) occlusion score decreased to 1 where tubules were fully occluded (100% of tubules occluded) at 12 weeks.

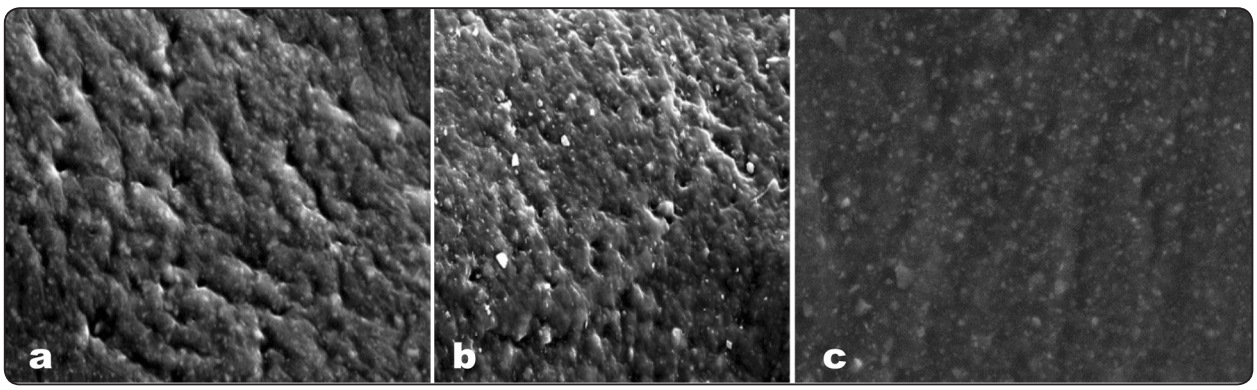


Fig. (3): a) Scanning electron microscopy (SEM) micrographs at magnification ×500 of inverse replica performed on hypersensitive areas of patients treated with BioMin TM C (group III) displaying occlusion score 5 (0%: no tubule occlusion) at baseline. b) occlusion score 4 where mostly of tubules unoccluded (25% of tubules occluded) at 3 weeks. c) occlusion score decreased to 3 where there were equally occluded/unoccluded tubules (50% of tubules occluded) at 6 weeks.

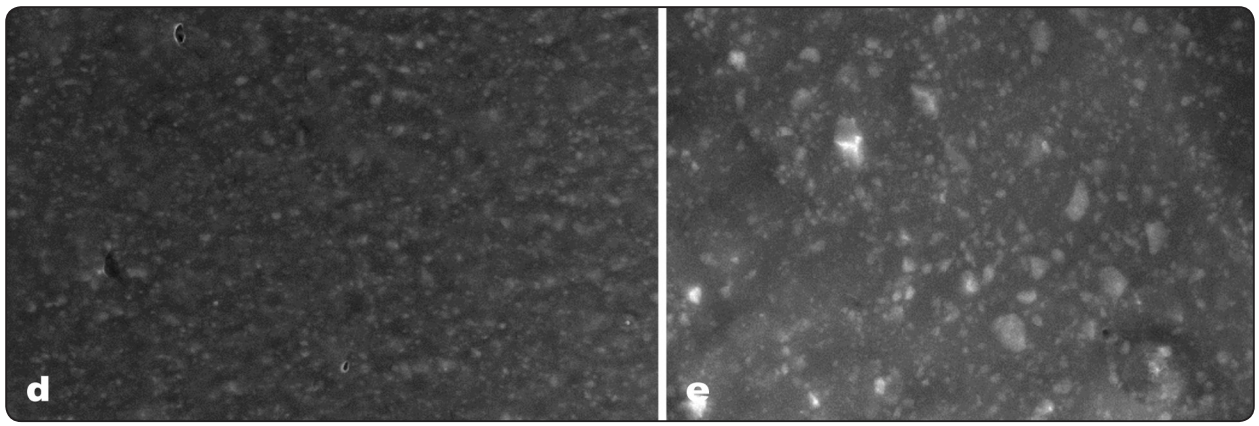


Fig. (3): d) occlusion score decreased to 2 where mostly of tubules occluded (75% of tubules occluded) at 9 weeks. e) occlusion score decreased to 1 where tubules were fully occluded (100% of tubules occluded) at 12 weeks.

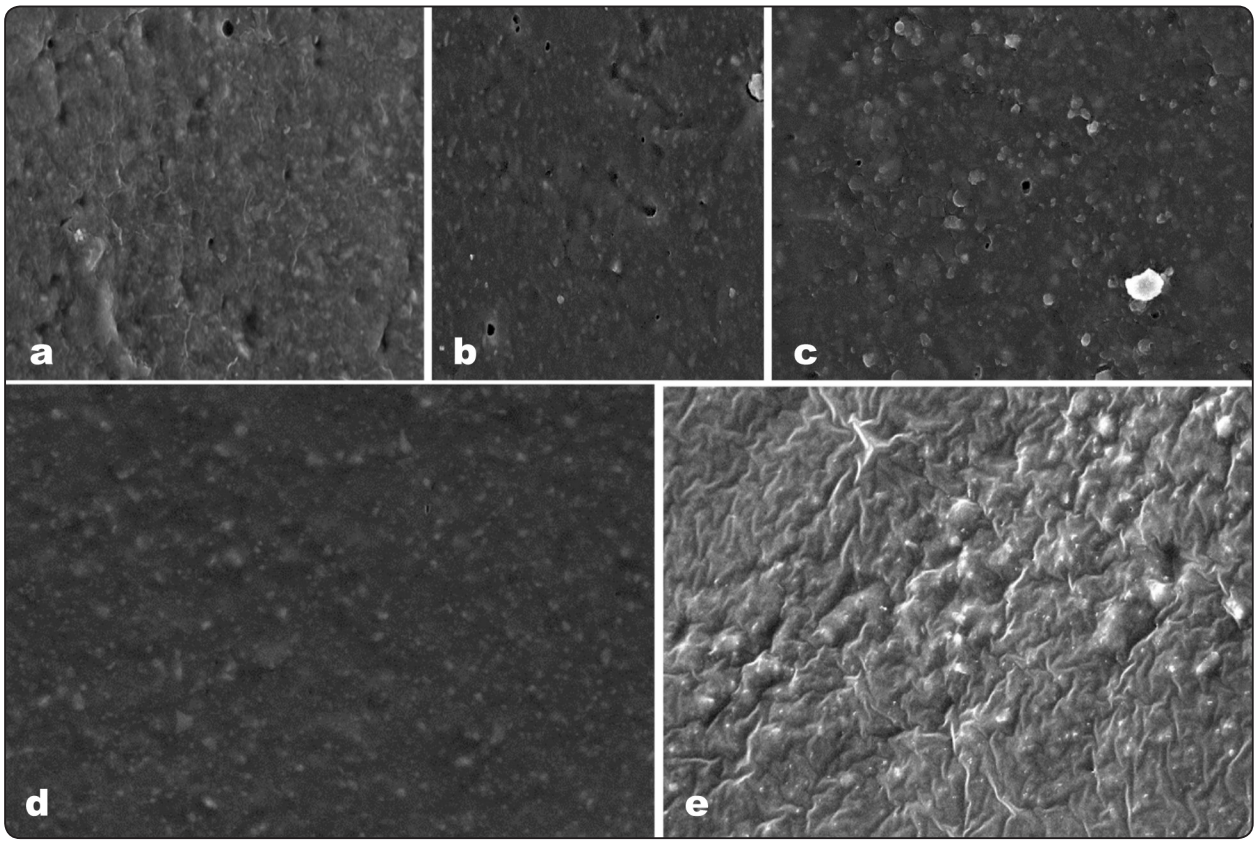


Fig. (4): a): Scanning electron microscopy (SEM) micrographs at magnification ×500 of inverse replica performed on hypersensitive areas of patients treated with Curodont TM D'senz (group IV) displaying occlusion score 4 where mostly of tubules unoccluded (25% of tubules occluded) at baseline. b) occlusion score decreased to 2 where mostly of tubules occluded (75% of tubules occluded) at 3 weeks. c), d) and e) occlusion score decreased to 1 where tubules were fully occluded (100% of tubules occluded) at 6,9 and 12 weeks.

## DISCUSSION

Dentin hypersensitivity is a prevalent oral problem[20]. It is based on an etiological factor removal, such as occlusal adjustment, dietary advice and/or tooth-brushing instructions. The successful treatment of dentin hypersensitivity improves both physical comfort and health-related quality of life highlighting the need to develop and assess effective therapeutic strategies [21].

Considering the complex and multifactorial etiology of dentin hypersensitivity, a number of home use and in-office therapeutic approaches have been developed with varied mechanisms of actions. Over the years, more attention has been provided to develop home-use interventions with various active compounds for the management of dentin hypersensitivity [1].

Fluoride gel with high fluoride content (12,500 ppm) was chosen as a treatment modality since it was found to be effective in permanently closing exposed dentinal tubules through deposition of particles on the surface of the dentin [9]. Bioactive glasses were another treatment modality that have a unique biological property of surface dissolution upon contact with body fluids, which results in the precipitation and crystallization of a biocompatible hydroxyapatite like layer. Accordingly, (BioMin™ F) and (BioMin™ C) regarded as biomimetic mineralizers matching the human body's own mineralizing traits and enhance the way saliva replaces lost mineral on tooth surfaces. BioMin™ C was designed for consumers wanting a high-performance fluoride free toothpaste, and for those regions where ground waters contain high rates of naturally occurring fluoride[10]. In addition, preself-assembling biomimetic peptides utilizing the P11-4-based Curolox technology was found to be effective in relieving dentin hypersensitivity due to biomatrix formation with high adhesion forming a stable, highly effective protective barrier on the tooth surface immediately after application [11]. Therefore, a current comparison of their abilities in the treatment of dentinal hypersensitivity through biomimetic mineralization was suggested to be of a clinical value.

In addition, Aquasil ULV® impression material recording replica impression was chosen as it utilizes the superior properties of both polyethers and additional curing silicones. These impression materials are able to capture an accurate impression of the tooth surface. The material portrays excellent reproduction of detail and good dimensional stability with snap set characteristics, high tear strength, and no swelling or shrinkage. In addition, these materials can be imaged directly without the need to cast positive replicas [12].

There was a variety of measurements for the painful responses. Gillam study [22] reported that mechanical, chemical, electrical and thermal stimulation can be used for pain assessment. Arising from the fact that different stimuli can elicit different pain sensations, at least two triggers of dentin hypersensitivity should be used in the clinical trial and in congruent with guidelines for conducting dentin hypersensitivity studies [23,24], two different assessment methodologies were described in present study; a subjective evaluation of pain produced by a defined stimulus (response-based assessment) through application of evaporative air-blast stimulus and a stimulus intensity required to provoke pain (stimulus-based assessment) utilizing electrical sensitivity stimulus.

Evaporative and electrical stimuli used for dentin hypersensitivity assessment were very accurate in reproducing the pain experienced by the patient in daily activities and were easy to apply. Evaporative test was considered the most common and validated stimulus used in clinical trials as its physiological and controllable as reported by Lin et al [25]. It involves a wide area of exposed dentin and acts promoting the evaporation of the fluid inside the tubules, thus reducing temperature at the dentin surface. This fact reduces pressure difference inside the tubule and consequently triggers the receptors in the pulp propitiating the pain sensation [26].

While, electrical sensitivity assessment through utilizing a digital electrical pulp tester has been used in the current study as it provides a simple, objective, standardized, reproducible and accurate way of assessing the condition of the pulp. The electrical stimulation was used as a stimulus source to compare the effects of dentin hypersensitivity mitigation before and after treatment which can be recorded numerically. It depends on ionic movement[27].

Currently, evaporative stimulus was applied first followed by electrical stimulus to avoid a negative impact on the results of the stimulation providing that the least severe stimulus was applied before the most severe, and to prevent interpretation error. In addition, five minutes were allowed between the two stimuli to allow for tooth recovery time as recommended by Hall C et al [14].

Visual analogue scale (VAS) was used to assess the patient perceived sensitivity in the current study since it is the most appropriate method to measure pain. In addition, this method has the advantage of being a continuous numerical scale that allows the conversion of the subjective response into objective data resulting in quantification of pain response. Furthermore, it has been shown to be efficacious, simple in application and accompanied by patient comprehension [28].

In addition, Schiff Sensitivity Scale was chosen currently based on its ability to assess the degree of dentinal hypersensitivity pain according to the patient stimulus reaction as reported by Fu Y et al [29]. This is congruent with Rocha CO et al [30], who found that, the Schiff sensitivity scale showed good results using tactile stimulus. The Schiff sensitivity scale was filled out by the operator to avoid interpretation and filling biases by the patient.

Moreover, this study thought to develop an accurate method of quantifying the degree of dentin tubule occlusion using negative replica technology. A scale of 1 (occluded) to 5 (un-occluded) to score the degree of tubule occlusion was used. This occlusion scale is commonly used for in situ studies where a broad range of occlusion scores are achieved [12].

The findings of the current study revealed that, all tested treatments were effective in reducing dentin hypersensitivity throughout the application protocol of clinical study regardless of the mechanism of action used and the results of current clinical study confirm those of previously published clinical studies that separately demonstrate the efficacy of each Elmex gel, BioMin™ F, BioMin™ C and Curodont™ D'senz in the treatment of dentin hypersensitivity.

Concerning the comparison between the efficacy of the four therapeutic materials during the experimental study period based on electrical sensitivity mean values. As there was a statistically significant difference among all tested groups at baseline, 3 and 12 weeks. An accepted explanation was highlighted by Cochrane review that discussed the possible imbalance between groups since (BioMin™ F) group recorded higher initial mean values of pain (16.86) compared to (7.29) of (Elmex Gele'e) group. This imbalance may have biased the results by reducing any observed difference in effects between groups. Also, this could be attributed to fluctuations of symptoms in sufferers and in studies such as this, participants are only eligible if they have marked sensitivity at the start of the study. For at least some of the participants this baseline sensitivity will be higher than their long-term average sensitivity and they are, therefore, likely to show improvements in dentin hypersensitivity pain over the course of the study as their sensitivity returns towards this average [31].

Concerning the comparison between the efficacy of the four therapeutic materials based on VAS score mean values, as there was a statistically significant difference among all tested groups at 3 ,6 and 9 weeks. The significant difference was found between group III versus group I and group II at 3 and 6 weeks indicating that patients treated with BioMin™ C showed significantly highest pain relief

compared to those treated with Elmex Gele'e and BioMin™ F at such assessment periods. This was confirmed by manufacturer conclusion who reported that, BioMin™ C glass material, a Chloride ion replaces the Fluoride ion incorporated in BioMin™ F then glass breaks down faster than the BioMin® F toothpaste formula to deliver hydroxyapatite onto the surface of the tooth. This was confirmed also by a previous study [32] who concluded that, upon comparison, the Biomin® containing dentifrice, showed better percentage of dentinal tubule occlusion as compared to Novamin® containing dentifrice and the fluoride control. This was true also in the current study showing that, at 6 weeks there was a significant difference between group III versus group IV denoting that patients treated with BioMin™ C exhibited significant reduction in dentinal hypersensitivity compared to those treated with Curodont TM D'senz at 6 weeks denoting the rapid action of BioMin™ C.

Generally, the results from the present in vivo study would appear to support the growing evidence in many published literatures that BioMin™ F and BioMin™ C may be an effective approaches treating dentin hypersensitivity following twice-daily tooth brushing. The clinical study indicated also successful pain relieve for Curodont™ D'senz in the treatment regimen. In addition, Fluoridation measures using Elmex Gele'e could represent an effective therapeutic approach. In addition, the reported effectiveness was maintained throughout the successive weeks of follow-up. These favorable outcomes can be attributed to the adherence of the patients to the proposed treatment plan. In addition, reduced symptoms in all groups clearly demonstrates that individuals participating in a clinical trial on dentinal hypersensitivity often show improvement in symptoms [33]. An explanation to this, the mere suggestion to a patient that a prescribed product is an effective treatment can bring about considerable improvement regardless of the formulation's therapeutic potential. Another probable factor may be the environment under which this study was performed. The patients knowingly participated in a clinical trial to determine the efficacy of desensitizing products. Despite randomization and stratification effects to homogenize sample characteristics, enrolled volunteers often try to please the investigators. Furthermore, positive emotional and motivational stimuli could activate the body's central pain-inhibiting system, which can modulate painful stimuli from the periphery through the release of endorphins centrally [34].

This together with the recognized impact of the placebo and Hawthorne effects on clinical study outcomes may contribute to the unexpected, inconsistent and somewhat contradictory findings often reported for dentin hypersensitivity studies. Up to 60% of the dentin hypersensitivity relief observed in clinical studies has been attributed to the placebo effect (a positive response arising from the action of intervention rather than an active ingredient) [35] as it can occur when there are excellent relations between the dentist and patient, spontaneous improvement, fluctuation of symptoms, regression to the mean, answers of politeness and conditioned answers. Furthermore, the Hawthorne effect (a change in subject behavior as a result of participating in an observed study or a response to non-intervention procedures) such as frequent examinations or improved oral hygiene will likely influence tooth brushing behavior leading to improved plaque control during study participation. Such improvements in oral hygiene during dentin hypersensitivity study would decrease the pain because this may allow greater saliva access to patent dentinal tubules which in turn may enhance tubule obliteration through greater deposition of salivary calcium, phosphate and proteins with increased contact between the saliva and the dentin surface, and thereby enhance the occlusion of patent dentinal tubules [34]. The presence of abrasives in the toothpaste may also have played a role in occluding the dentinal tubules. Any one of these factors, or a combination of the above, could be responsible for the unexpected improvements in sensitivity reported in this study.

The scanning electron microscope analysis showed that, occlusion scores values fell markedly from baseline to subsequent follow ups and there was an increase in the percentage of dentinal tubule occlusion in all groups which were statistically significant. It is worth noting that occlusion of dentin tubules leads to an inhibition of the cascade from external stimuli directly to the pulp in which the stimulation of the mechanoreceptors does not occur, thus preventing the pain response. On the other hand, it is recognized that the quantification of the number of occluded tubules is somewhat subjective [36]. Nevertheless, the observations from the current SEM indicated that there was a degree of tubular occlusion which varied between the tested materials.

Based on the current findings, it is important to high lighten some facts regarding dentin hypersensitivity measurement and assessment. It was reported that it is subjected to psychological interference and difficult to objectively measure and evaluate. In addition, responses to various stimuli can differ. The different number of included studies for each stimulus, different active ingredients involved, and different number of patients may play a role in differing responses of each active ingredient per stimulus. In addition, response to treatment is based on the patients' subjective assessments of the severity of the condition. This has obvious drawbacks, particularly in relation to emotional effects on the patient's perception of pain at any given time, which can differ from person to person, between sex, gender and age, and also, from one day to another. In spite of this scattered effect in the patients' perception of pain, and therefore a weakness when comparing similar clinical trials, we were able to report similar results as previously published studies [37].

The concept of biomimetic mineralization has focused on permeant long-term management of dentin hypersensitivity. Therefore, the therapeutic approaches of these tested materials on non- carious cervical lesions are in accordance with this concept.

## CONCLUSION

**Under the limitations of this study it could be concluded that;**

1. There was a remarkable pattern of reduction of dentin hypersensitivity symptoms with time for all the assessment clinical parameters during the treatment period of the study independent of treatment groups or strategies that proves the clinical efficacy of the tested materials.
2. The therapeutic approach of the different tested materials on non-carious cervical lesions had focused on successful permanent long-term management of dentin hypersensitivity.
3. The impression material used for replica was able to reproduce different degrees of tubule occlusion in the clinical environment and it was easy to repeatedly revisit designated areas on the tooth surface.

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