

 *nanoXIM*
CAREPASTE



EXECUTIVE FILE

Summary

nanoXIM•CarePaste is a synthetic nano-hydroxyapatite aqueous paste for Oral Care applications, manufactured by FLUIDINOVA, S.A. in Portugal.

Dental cavity and hypersensitivity prevention, pain reduction, and enamel remineralization are the main benefits of this ingredient.

nanoXIM•CarePaste also contributes to a smooth and protected tooth surface, restoring its natural whiteness.

nanoXIM•CarePaste is the recommended ingredient for aqueous formulations, and can be incorporated in toothpastes, mouthwashes, gels, dental floss and other oral care products (personal and professional use).

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Dental Hypersensitivity

In vitro study 1

This *in vitro* study compares Aclaim toothpaste (Group Pharmaceuticals Ltd., India), a dentifrice containing 6.5% nanoXIM•CarePaste, with Colgate Pro-Relief™ Pro-Argin™ technology.

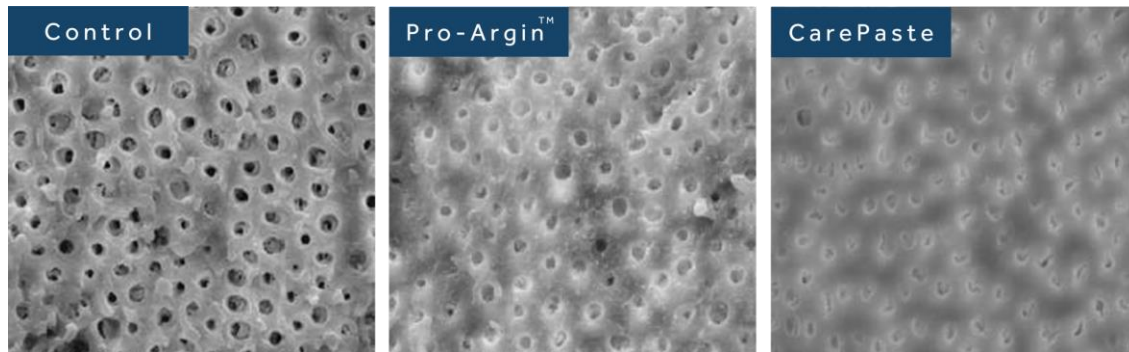


Figure 1: Effect of Colgate Pro-Relief™ and nanoXIM•CarePaste-based toothpaste on dentin tubule occlusion after two minutes of treatment. A sample without treatment (control) was also analyzed. Data gently provided by Group Pharmaceuticals Ltd., India.

- ✓ The Aclaim toothpaste (that contains nanoXIM•CarePaste) led to a high degree of tubule occlusion after just two minutes, which was five times faster than the occlusion rate seen with Colgate Pro-Relief™.

In vitro study 2

The purpose of this study was to evaluate the effect of three different desensitizing agents: 6.5% nanoXIM•CarePaste (Aclaim Toothpaste, Group Pharmaceuticals, Ltd., India), 5% NovaMin (Shy NM toothpaste, Group Pharmaceuticals, Ltd., India) and 8% Pro-Argin™ (Colgate sensitive pro-relief toothpaste, Colgate-Palmolive India Ltd., India).

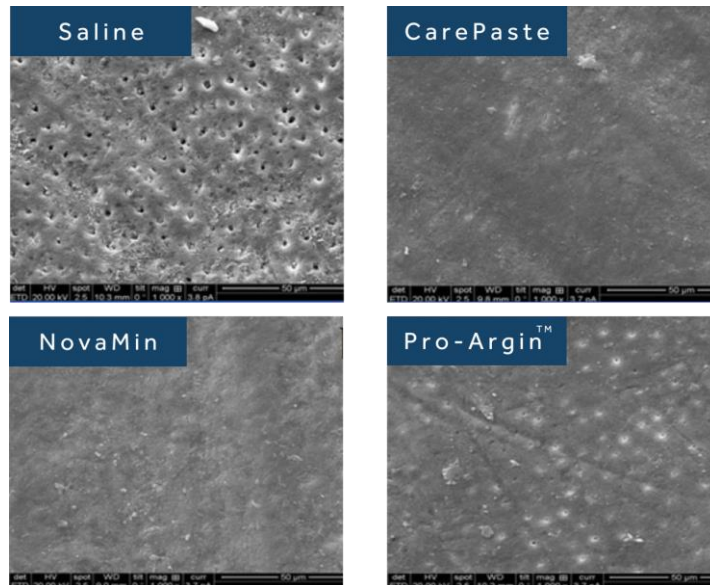


Figure 2: Scanning Electron Microscopy images of dentin discs treated daily with saline solution (negative control), nanoXIM•CarePaste, NovaMin and Pro-Argin™ for two minutes, for seven days.

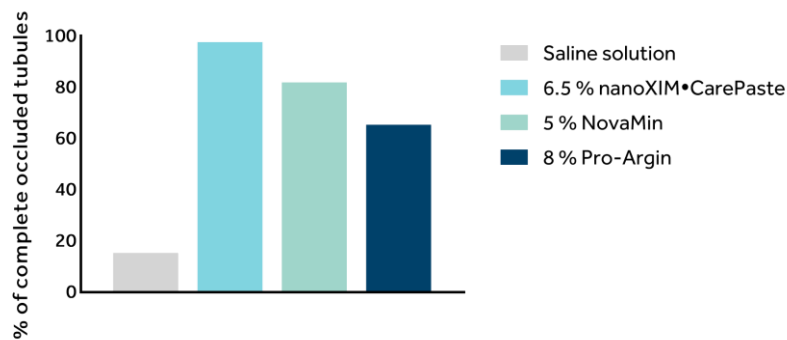


Figure 3: Percentage of completely occluded dentin tubules after seven days of treatment (a two-minute daily treatment) with the different desensitizing agents.

- ✓ nanoXIM•CarePaste was the most effective desensitizing agent of this study, in comparison with NovaMin and Pro-Argin™ ingredients, showing almost complete tubule occlusion during the treatment period;
- ✓ A two-minute daily treatment for seven days with nanoXIM•CarePaste allowed 98% of completely occluded dentin tubules, in opposition to NovaMin and Pro-Argin™, with 82% and 65%, respectively.

In vitro study 3

This study compared the effectiveness of four different dentifrices for dentin tubule occlusion: Pepsodent Pro-sensitive relief and repair, Sensodyne repair and protect, Remin Pro and a toothpaste containing 15% nanoXIM•CarePaste. The mean percentage of dentin tubule occlusion was determined by observation using scanning electron microscopy (SEM).

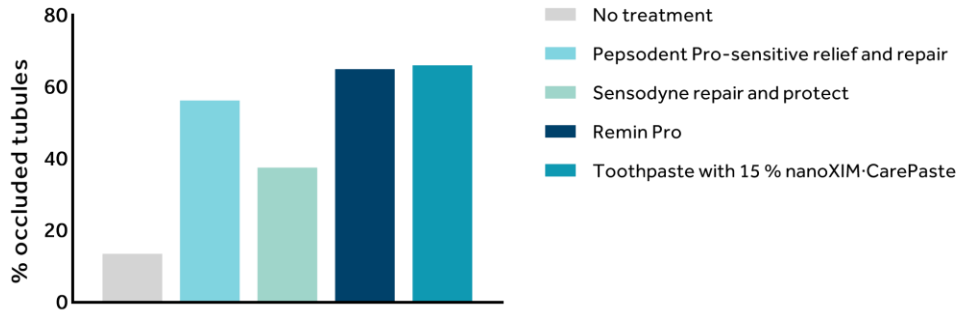


Figure 4: Mean percentage of occluded tubules after a daily treatment of two minutes, during fourteen days.

- ✓ The toothpaste containing 15% nanoXIM•CarePaste allowed the highest percentage of dentin tubule occlusion, corresponding to 66.13%, followed by Remin Pro (65.04%) and Pepsodent Pro-sensitive relief and repair (56.28%);
- ✓ These results encourage the usage of a toothpaste containing 15% nanoXIM•CarePaste for the treatment of dentin hypersensitivity, as a two-minute daily application for fourteen days allows a significant occlusion of dentin tubules.

In vivo clinical study 1

An *in vivo* clinical study of forty-five patients was performed to test the efficacy of Aclaim toothpaste (Group Pharmaceuticals, Ltd., India) containing 6.5% nanoXIM•CarePaste, Sensodent-K toothpaste (potassium nitrate) and a propolis dentifrices in controlling dental hypersensitivity.

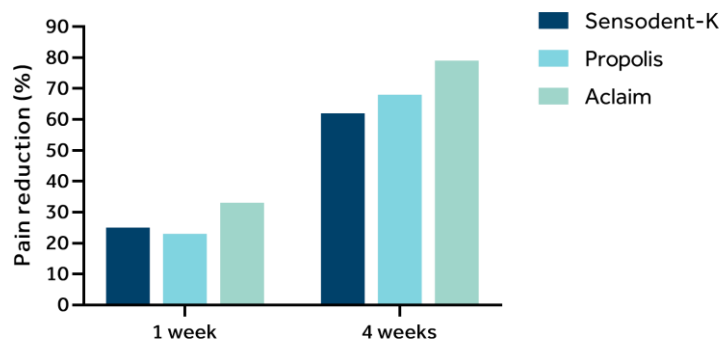


Figure 5: Reduction of dental hypersensitivity after treatment with Sensodent-K (potassium nitrate), Propolis and Aclaim (nanoXIM•CarePaste) during one and four weeks.

- ✓ Immediately after one week of treatment, a pain reduction of approximately 35% was observed among the patients treated with the nanoXIM•CarePaste. In opposition, the dentifrices containing potassium nitrate and propolis only decreased the hypersensitivity by 25%;
- ✓ The dentifrice containing nanoXIM•CarePaste was the most efficient in reducing dental hypersensitivity, allowing superior pain relief after one and four weeks of treatment with a final pain reduction of up to 80%.

In vivo clinical study 2

In this study, it was compared the effectiveness of three dentifrices containing three different ingredients in reducing dental hypersensitivity:

1. Nano-hydroxyapatite (nanoXIM•CarePaste) (Aclaim, Group Pharmaceuticals, India);
2. Calcium Sodium Phosphosilicate (NovaMin) (SHY-NM, Group Pharmaceuticals, India);
3. Casein Phosphopeptide (CPP) – Amorphous Calcium Phosphate (ACP) (G. C. Tooth Mousse, Recaldent, Australia).

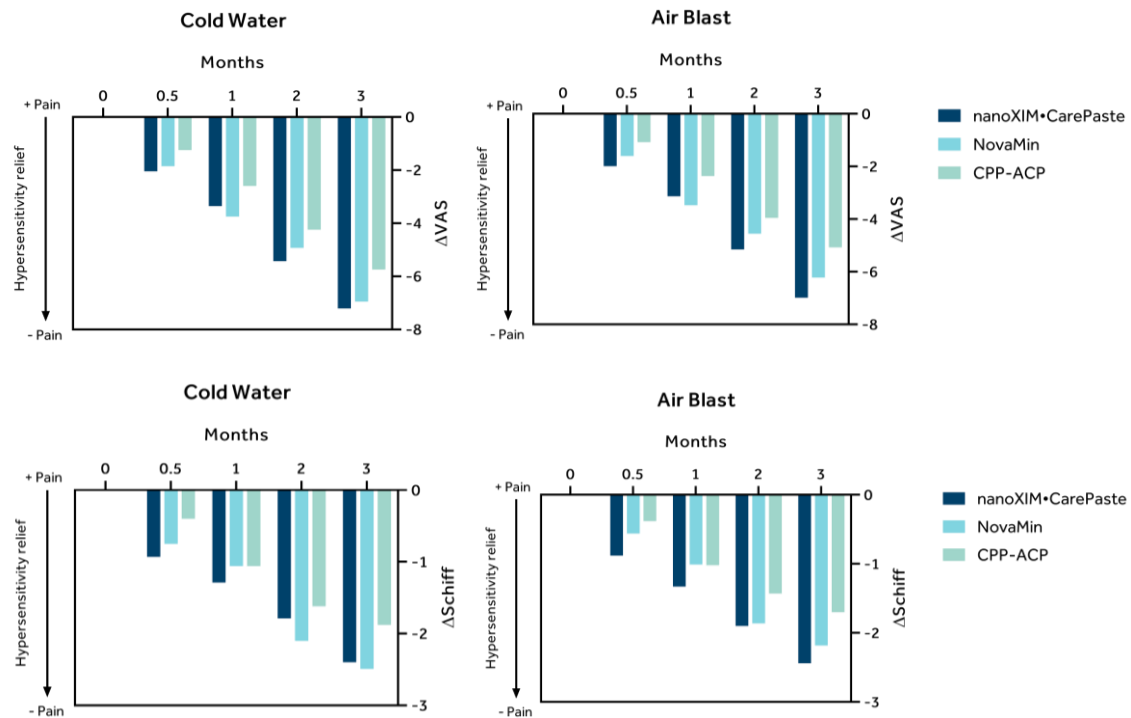


Figure 6: Hypersensitivity reduction for the three toothpastes with different ingredients tested using the VAS score and Schiff test. For each time point, it was calculated the difference from the baseline.

- ✓ In 100% of the cases, the toothpaste containing nanoXIM•CarePaste performed better than the CPP-ACP toothpaste;
- ✓ In 75% of the cases, nanoXIM•CarePaste toothpaste performed better than the NovaMin toothpaste;
- ✓ Immediately after two weeks of treatment, the nanoXIM•CarePaste toothpaste systematically provided superior pain relief when compared with NovaMin and CPP-ACP toothpastes.

In vivo clinical study 3

In the present clinical trial, it was evaluated the efficacy of dental hypersensitivity reduction of PrevDent toothpaste (PrevDent B.V., Netherlands) containing 15% nanoXIM•CarePaste ingredient, in comparison with a fluoride toothpaste (positive control) and a negative control placebo dentifrice (glycerin and water).

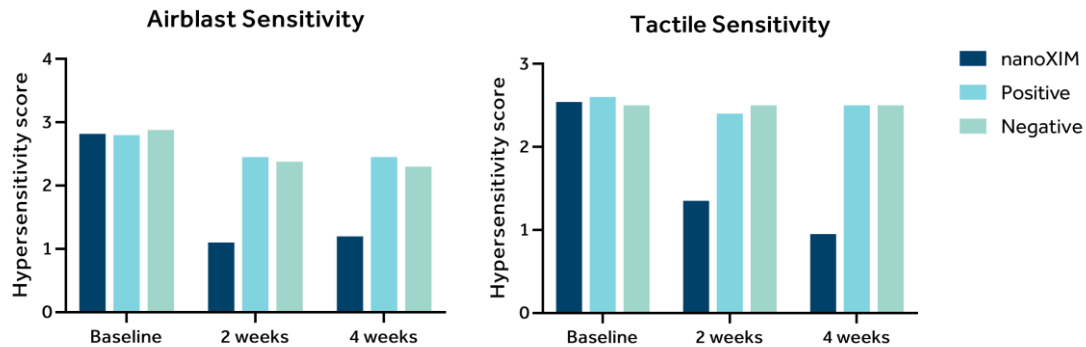


Figure 7: Hypersensitivity scores for the three different group treatments and for both stimuli tests (air blast and tactile) at baseline, two and four weeks of treatment. nanoXIM: experimental group (nanoXIM•CarePaste toothpaste). Pos: positive group (fluoride toothpaste). Neg: negative group (placebo toothpaste).

- ✓ PrevDent toothpaste containing nanoXIM•CarePaste performed better than Colgate fluoride toothpaste for both air blast and tactile sensitivity tests in a statistically significant way ($P < 0.001$);
- ✓ For the air blast stimulus, the PrevDent toothpaste containing 15% of nanoXIM•CarePaste was capable of decreasing dental hypersensitivity by 61% immediately after two weeks. In opposition, the Colgate toothpaste containing fluoride was only capable to reduce hypersensitivity by 13%;
- ✓ For the tactile stimulus, it was verified a 47% hypersensitivity reduction after 2 weeks and a final hypersensitivity reduction of 63% after four weeks of treatment with a 15% nanoXIM•CarePaste toothpaste from PrevDent.

In vivo clinical study 4

In this clinical trial, it was compared the efficacy of a dentifrice containing 6.5% nanoXIM•CarePaste (Aclaim toothpaste, Group Pharmaceuticals, Ltd., India) with Sensodent-KF (Indoco Remedies Ltd., India), a fluoridated desensitizing toothpaste used for the management of dentinal hypersensitivity.

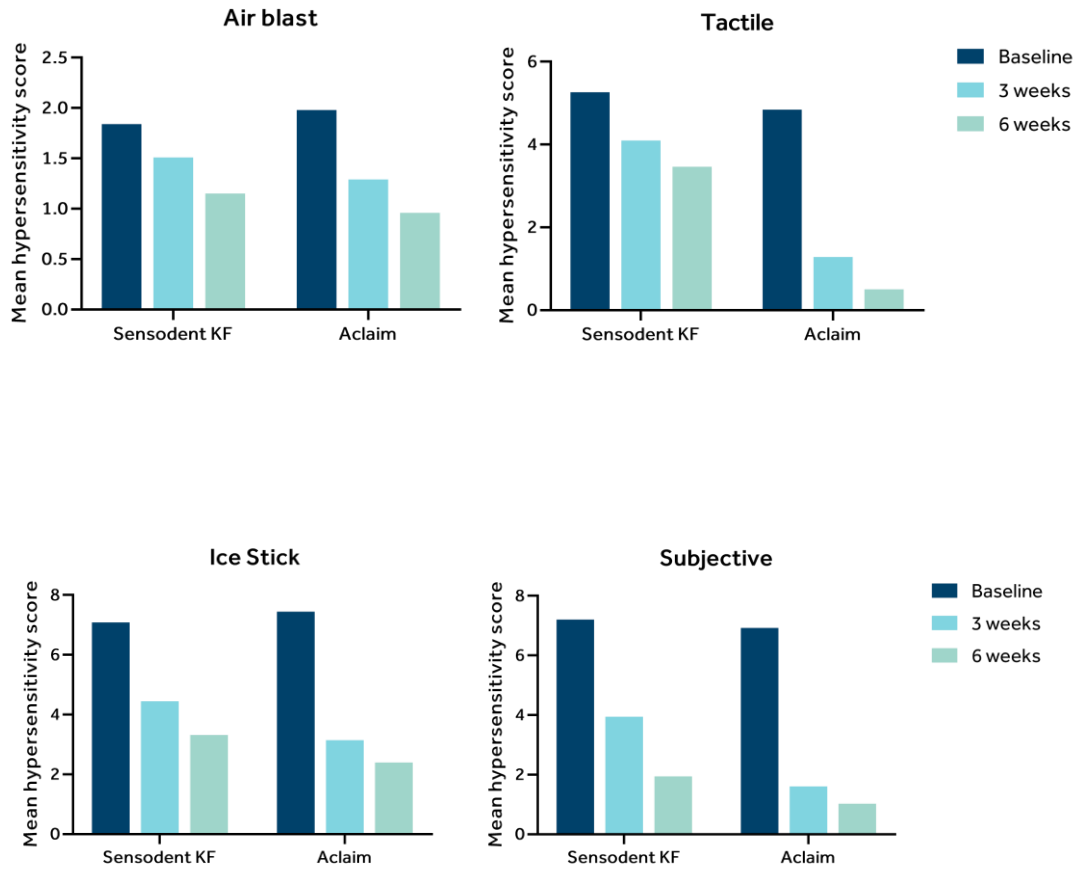


Figure 8: Mean hypersensitivity scores obtained for the subjects treated with Sensodent-KF and Aclaim toothpaste. The scores were measured after four different stimuli (air blast, tactile, ice stick and subjective) at the baseline, 3 and 6 weeks.

- ✓ Aclaim toothpaste containing nanoXIM•CarePaste allowed a superior hypersensitivity reduction for all the stimuli tested after three and six weeks of treatment.

Source: P. Verma, U. Gupta, V. Dodwad, B. Kukreja, K. Arora. Evaluation of the Clinical Efficacy of a new Desensitizing Tooth Paste Containing Nano-crystalline Hydroxyapatite in Dentine Hypersensitivity Patients: A Double Blind Randomized Controlled Clinical Trial. Journal of Dental Specialities. 1(2), p. 47, (2013) LINK

In vivo clinical study 5

In this study, thirty patients diagnosed with dental hypersensitivity were treated with a commercially available toothpaste (Aclaim, Group Pharmaceuticals, Ltd., India) containing 6.5% nanoXIM•CarePaste. The patients were instructed to use the toothpaste twice a day and the treatment was performed during six months, with follow-up observations at one and three months.

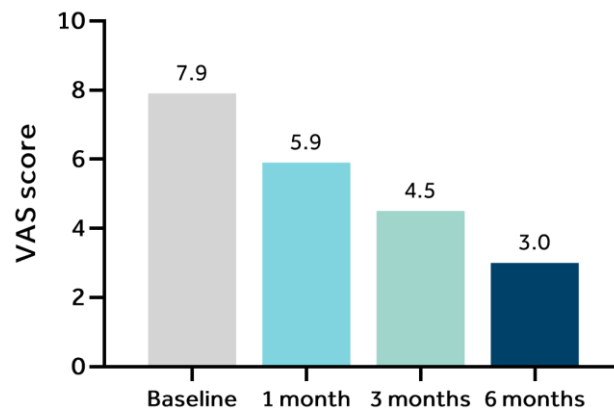


Figure 9: Hypersensitivity mean scores measured at baseline, one, three and six months after treatment, with Aclaim toothpaste (containing 6.5% nanoXIM•CarePaste).

- ✓ After one month of treatment, the patients treated with the Aclaim toothpaste containing nanoXIM•CarePaste experienced a pain reduction of 26%;
- ✓ An average hypersensitivity reduction of 62% was obtained after six months of treatment.
- ✓ On average, the regular use of a toothpaste containing nanoXIM•CarePaste allowed to reduce in six months from severe and intense pain to a mild level of pain.

In vivo clinical study 6

The objective of this trial was to evaluate the efficacy of three different desensitizing toothpastes containing NovaMin (Vantex toothpaste), Arginine (Colgate Sensitive Pro-Relief®) and nanoXIM•CarePaste (test toothpaste). The clinical study was performed in forty-five patients and the sensitivity was measured immediately after a single application and at one- and four-week follow-up.

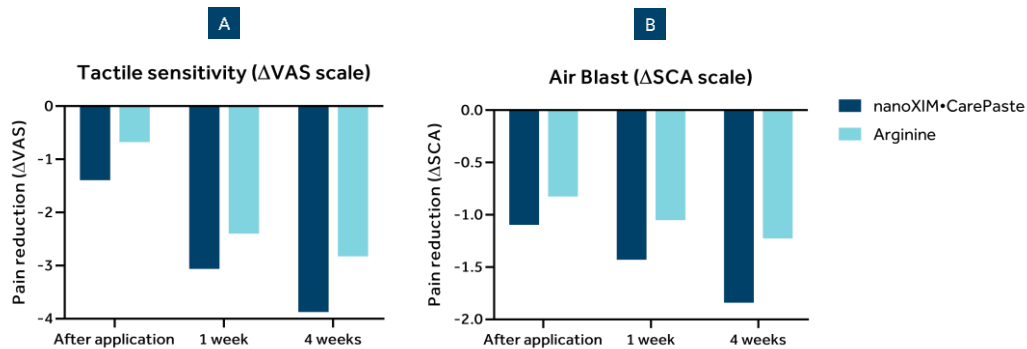


Figure 10: A: Improve in hypersensitivity reduction using tactile sensitivity assessment (Δ VAS scale) obtained for nanoXIM•CarePaste vs. NovaMin (Δ VAS_{nanoXIM} - Δ VAS_{NovaMin}) and Arginine vs. NovaMin (Δ VAS_{Arginine} - Δ VAS_{NovaMin}).

B: Improve in hypersensitivity reduction using air blast assessment (Δ SCA scale) obtained for nanoXIM•CarePaste vs. NovaMin (Δ SCA_{nanoXIM} - Δ SCA_{NovaMin}) and Arginine vs. NovaMin (Δ SCA_{Arginine} - Δ SCA_{NovaMin}). The scores were measured immediately after a single application and at one- and four-week follow-up.

	After Application		1 week		4 weeks	
	Difference in Δ VAS	Difference in Δ SCA	Difference in Δ VAS	Difference in Δ SCA	Difference in Δ VAS	Difference in Δ SCA
nanoXIM vs NovaMin	14%	11%	31%	14%	39%	18%
nanoXIM vs Arginine	7%	8%	24%	11%	28%	12%

Table 1: Pain reduction expressed in the difference between Δ VAS and Δ SCA for nanoXIM•CarePaste versus NovaMin and nanoXIM•CarePaste versus Arginine.

- ✓ In this clinical trial, nanoXIM•CarePaste was the toothpaste ingredient that allowed superior pain relief when compared with Arginine and NovaMin in all the time points analyzed;
- ✓ Immediately after the application, nanoXIM•CarePaste showed a pain reduction 14% higher than NovaMin and 7% higher than Arginine for tactile sensitivity;
- ✓ For the tactile measurement, nanoXIM•CarePaste was 39% more effective than NovaMin and 28% more than Arginine after four weeks;
- ✓ For the air blast assessment, nanoXIM•CarePaste performed 18% better than NovaMin and 12% better than Arginine after four weeks.

Dental sensitivity is a frequent complication after tooth bleaching. The goal of this study was to verify if nano-hydroxyapatite (nHAp) was able to reduce tooth sensitivity associated with bleaching. For that purpose, it was compared the effect of 6% hydrogen peroxide (HP) bleaching agent with and without 2% nHAp (13% nanoXIM•CarePaste). This study shows that the presence of nano-hydroxyapatite reduced the sensitivity associated with the bleaching procedure and it did not interfere with the HP whitening treatment.

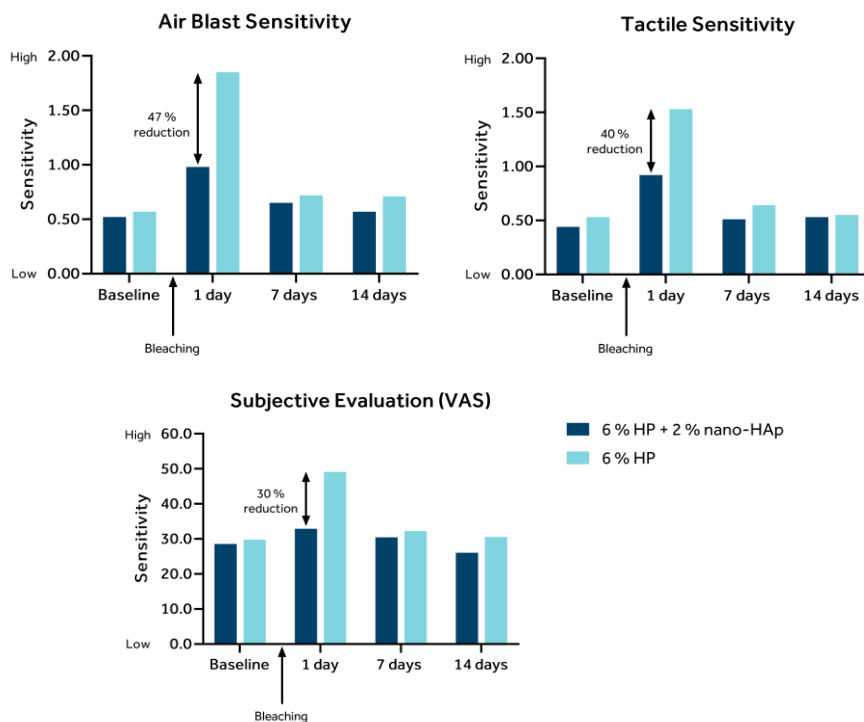


Figure 11: Sensitivity experienced by the patients treated with 6% HP and 6% HP + 2% nHAp, before bleaching and after one, seven and fourteen days of treatment. The sensitivity was assessed by air blast, tactile and subjective evaluation tests.

- ✓ For all the sensitivity tests performed and time points analyzed, the patients treated with 2% nHAp experienced less sensitivity than the patients treated only with 6% HP;
- ✓ For the Air Blast Sensitivity test, the patients treated with 6% HP + 2% nHAp felt 47% less sensitivity one day after bleaching, in comparison with the patients treated with 6% HP;
- ✓ After fourteen days of treatment, all tests showed higher sensitivity reduction for the patients treated with 6% HP + 2% nHAp versus the 6% HP, namely 20% (Air Blast), 4% (Tactile) and 15% (Subjective Evaluation).

Source: M. Vano, G. Derchi, A. Barone, A. Genovesi, U. Covani, "Tooth bleaching with hydrogen peroxide and nano-hydroxyapatite: A 9-month follow-up randomized clinical trial.", *International Journal of Dental Hygiene*, 13(4), p. 301 (2015). [LINK](#)

In vivo clinical study 8

The present clinical study was performed to investigate the efficiency of a commercial toothpaste in reducing dental hypersensitivity in adults. The main ingredients of this toothpaste are nano-hydroxyapatite (5% nanoXIM•CarePaste), potassium nitrate and sodium monofluorophosphate, along with antioxidants, phloretin, ferulic acid and silymarin. The patients were instructed to use this toothpaste at least once a day for two weeks. Moreover, they were asked to evaluate the degree, duration, intensity, tolerability and description of pain at baseline, two days and two weeks after treatment. This study revealed that the mentioned toothpaste significantly reduced pain associated with hypersensitivity when applied daily.

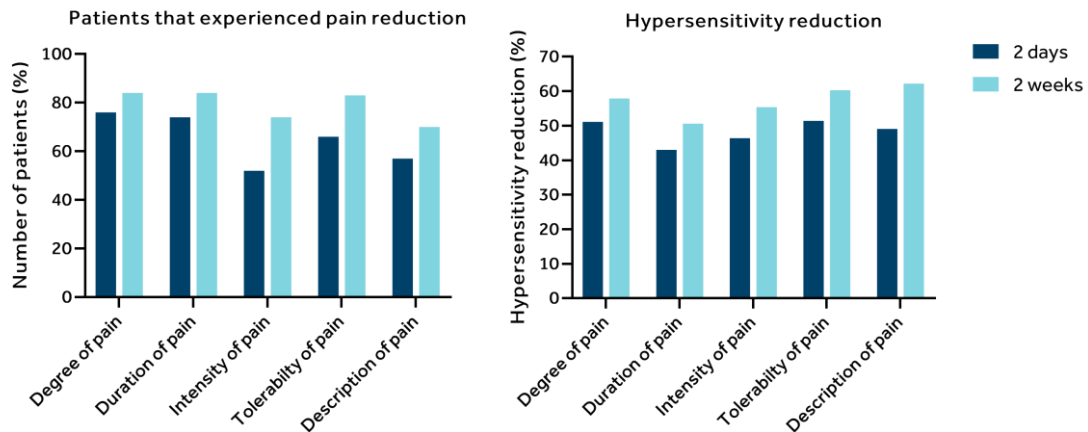


Figure 12: Percentage of the number of patients that experienced pain reduction (left) and the corresponding percentage of hypersensitivity reduction (right), after two days and two weeks of use. These patients presented moderate to severe hypersensitivity at the baseline and showed an improvement of at least 10% on the VAS scale.

- ✓ After two days of treatment, 52 to 76% of the patients experienced pain reduction in terms of degree, duration, intensity and tolerability of pain. Considering the description of pain, in which patients describe the pain from "no pain" to "shooting pain", the number of patients that felt reduction was 57%;
- ✓ Two weeks after treatment, 70 to 84% of the patients felt hypersensitivity reduction for all the questions asked;
- ✓ The percentage of hypersensitivity reduction felt by those patients was 43 to 51% after two days and 51 to 62% after two weeks.

In vivo clinical study 9

This study aimed to compare the efficacy of a single application of plain nano-hydroxyapatite (nHAp - nanoXIM•CarePaste) paste in reducing dentine hypersensitivity. For that, sixty-three patients were recruited and randomized to be allocated into three groups (n=21): Group 1 – nHAp paste, Group 2 – fluoride paste, and Group 3 – placebo. The patient's response to dentin hypersensitivity (DH) was evaluated at baseline (T0), immediately after application (T1), and after one week (T2).

Groups	Assessment Period	TS	CAS	VAS
Group 1: nHAp	T0	1.14±1.04 ^a	2.27±0.46 ^a	63.64±22.79 ^a
	T1	0.41±0.67 ^b	0.86±0.71 ^b	23.86±21.10 ^b
	T2	0.18±0.50 ^b	0.55±0.80 ^b	14.77±23.98 ^c
Group 2: Fluoride	T0	1.57±1.08 ^a	2.52±0.51 ^a	72.62±27.28 ^a
	T1	0.86±0.73 ^b	1.38±0.86 ^b	36.90±26.95 ^b
	T2	0.67±0.80 ^b	1.10±1.0 ^b	32.14±32.73 ^b
Group 3: Placebo	T0	1.29±0.10 ^a	2.48±0.51 ^a	71.43±25.35 ^a
	T1	0.48±0.60 ^b	1.05±0.97 ^b	27.38±26.11 ^b
	T2	0.76±0.70 ^b	1.48±0.60 ^b	38.10±15.04 ^b

Table 2: Mean tactile sensitivity (TS), cold air sensitivity (CAS) and visual analog scale (VAS) test scores of the groups.

- ✓ From T0–T1 and T0–T2, all three groups showed a statistically significant reduction in tactile sensitivity, cold air sensitivity, and visual analog scale scores ($P < 0.005$);
- ✓ From T1–T2, there was no significant reduction in the tactile sensitivity, cold air sensitivity, and visual analog scale scores of the groups ($P > 0.005$), except for nHAp, which showed a significant reduction ($P = 0.033$) in visual analog scale scores from T1–T2;
- ✓ At T2, the intergroup comparison demonstrated a significant difference in tactile scores ($P = 0.005$), cold air sensitivity ($P < 0.001$), and visual analog scale scores ($P < 0.001$).
- ✓ The single application of the nHAp paste (nanoXIM•CarePaste) showed a significant reduction in visual analog pain scores after one-week.

Enamel Remineralization

In vitro study 1

An *in-vitro* study was performed to test the remineralization potential of Aclaim toothpaste (Group Pharmaceuticals Ltd., India) containing 6.5% nanoXIM•CarePaste ingredient with a Casein PhosphoPeptide-Amorphous Calcium Phosphate (CPP-ACP) dentifrice.

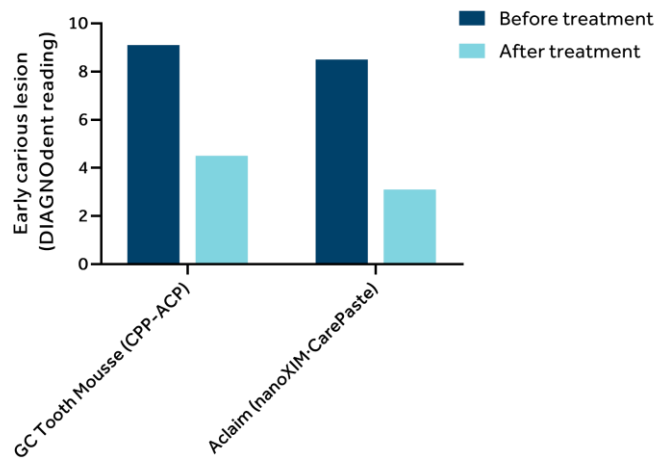


Figure 13: nanoXIM•CarePaste has a greater effect than CPP-ACP dentifrice in remineralizing the early carious lesion.

- ✓ Due to its similarity with natural enamel, nanoXIM•CarePaste promotes crystal growth and its integrity, helping to create a new crystalline and remineralized surface;
- ✓ In this study, nanoXIM•CarePaste was significantly more effective at remineralizing the carious lesion than the CPP-ACP dentifrice.

The goal of this study was to evaluate the potential of VITIS Whitening toothpaste (Dentaid S.L., Spain) containing 3% of nanoXIM•CarePaste in the remineralization of the enamel and dentin.

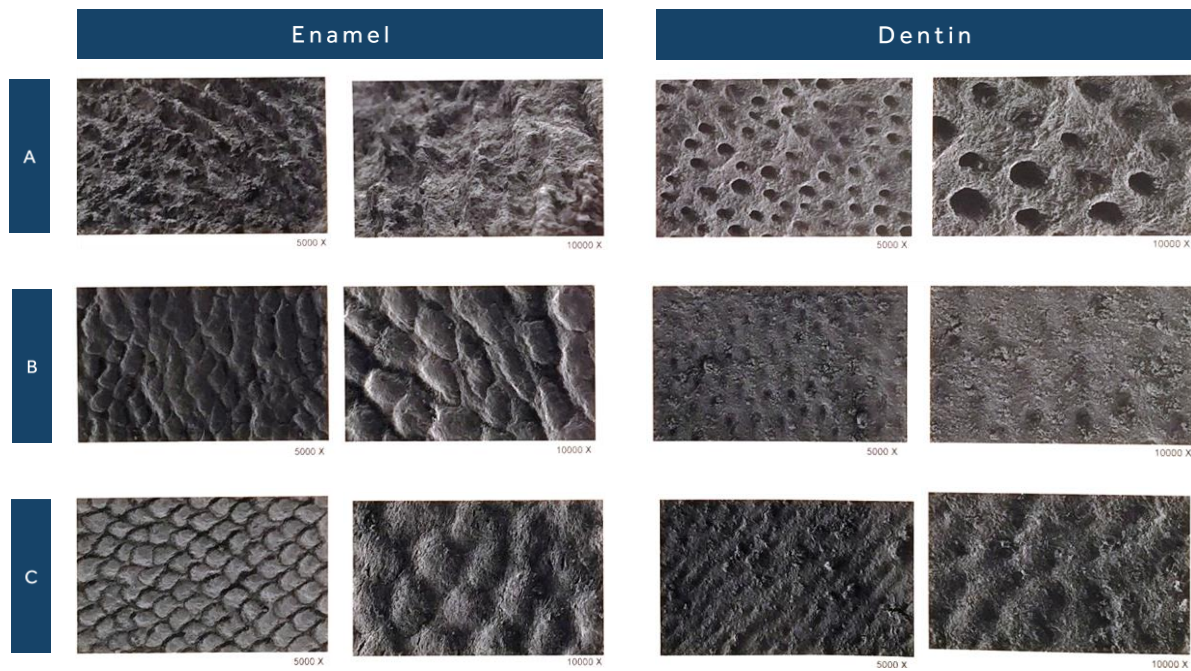


Figure 14: A: demineralized enamel and dentine with orthophosphoric acid at 37%;
 B: remineralized enamel and dentine after four days of treatment with nHAp toothpaste, twice a day for 4 minutes;
 C: after treatment, specimens were placed in contact with Coca-Cola® (pH = 2.52) for four minutes, twice a day for four days.

- ✓ A four-day treatment with VITIS Whitening toothpaste (containing 3% nanoXIM•CarePaste) effectively remineralized the enamel and dentin after their previously demineralization with orthophosphoric acid;
- ✓ The remineralized effect was maintained even after a four-day treatment with Coca-Cola®.

Source: Soler Ollé A, Massoli A, León R, Blanc V. Evaluación in vitro del efecto remineralizante de un dentífrice con nanopartículas de hidroxapatita, monofluorofosfato de sodio y xilitol. 49ª Reunión Anual SEPA, Barcelona, Spain. 2015. [LINK](#)

In vitro study 3

M. J. Ochoa (2015) evaluated the remineralization potential of three different concentrations of nanoXIM•CarePaste. For that purpose, bicuspid teeth were previously demineralized using 15% phosphoric acid for fifteen minutes. After demineralization, teeth were placed in aqueous solutions containing 5, 10 and 15% of nanoXIM•CarePaste for six and twelve days. After treatment, teeth were analyzed with Scanning Electron Microscopy (SEM), to observe the enamel surface and evaluate its remineralization.

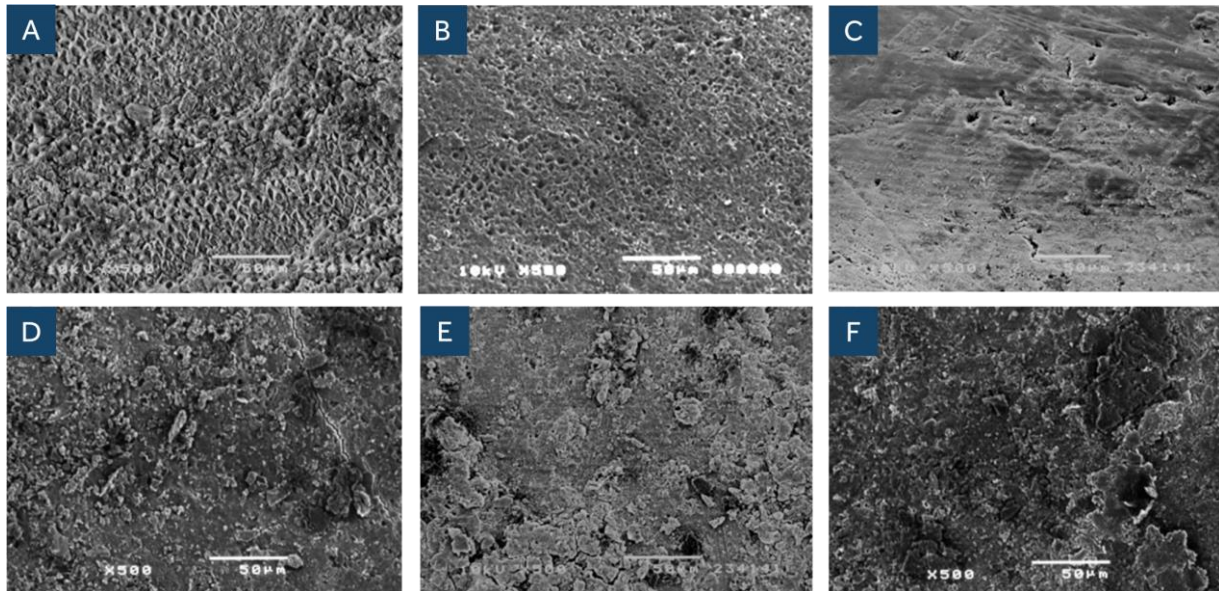


Figure 15: A: Demineralized enamel with pores created by phosphoric acid and without being treated with nanoXIM•CarePaste;
 B: Enamel treated with 5% nanoXIM•CarePaste for six days;
 C: Enamel treated with 5% nanoXIM•CarePaste for twelve days;
 D: Enamel treated with 10% nanoXIM•CarePaste for six days;
 E: Enamel treated with 10% nanoXIM•CarePaste for twelve days;
 F: Enamel treated with 15% nanoXIM•CarePaste for six days.

- ✓ nanoXIM•CarePaste was able to remineralize the enamel surface of previously demineralized teeth for all the concentrations tested, with pores being sealed by the hydroxyapatite nanoparticles;
- ✓ A concentration of 10% of nanoXIM•CarePaste was considered ideal as it was possible to achieve high remineralization within only six days. Therefore, nanoXIM•CarePaste can be used to remineralize the typical white spots formed after orthodontic treatments;
- ✓ A longer exposure to nanoXIM•CarePaste resulted in greater sealing of the pores and promoted superior enamel remineralization.

In vitro study 4

In the present study, it was compared the efficiency of four toothpastes in inhibiting demineralization adjacent to orthodontic brackets *in vitro*. The tested toothpastes were Aclaim (6.5% nanoXIM•CarePaste, Group Pharmaceuticals, India), Apagard (nano-hydroxyapatite, Sangi, Japan), Clinpro Tooth Crème (Tricalcium phosphate and fluoride, 3M ESPE) and Colgate Total (Fluoride, Colgate-Palmolive Company, India). For that purpose, stainless steel brackets were applied on healthy maxillary first premolars. After thirty-one days of daily treatment with each toothpaste, the brackets were removed and the teeth were observed under a polarized light microscope. The depths of demineralized enamel were measured in three different sites of gingival demineralized area: gingival margin, middle third and occlusal margin.

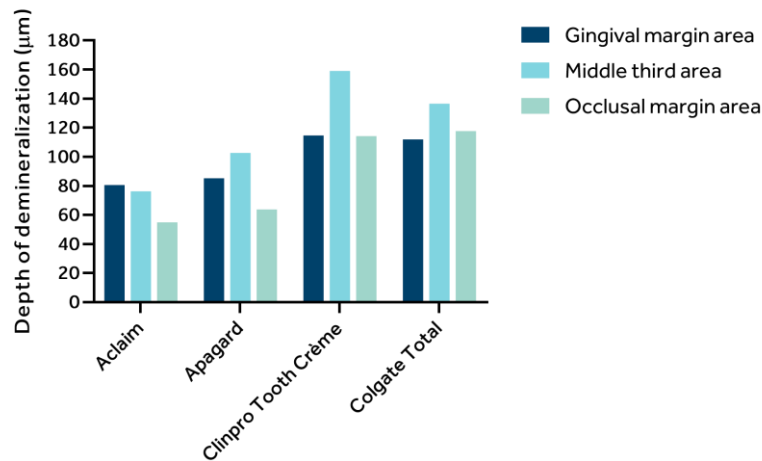


Figure 16: Site-specific comparison of depth of demineralization of each toothpaste tested. Lower values represent less demineralization.

- ✓ The Clinpro Tooth Crème and Colgate Total toothpastes were the less successful to inhibit enamel demineralization, in opposition to nano-hydroxyapatite-containing toothpastes;
- ✓ Comparing the two toothpastes that contain nano-hydroxyapatite (Aclaim and Apagard), Aclaim containing nanoXIM•CarePaste was more effective at reducing demineralized areas;
- ✓ The daily application of a toothpaste with nanoXIM•CarePaste provided higher protection against enamel demineralization in orthodontics.

In vitro study 5

P. Madhusudanan (2018) evaluated and compared the microhardness of artificially demineralized human enamel treated with three different remineralizing agents (potassium nitrate-containing toothpaste, casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) containing toothpaste and Aclaim toothpaste (Group Pharmaceuticals Ltd., India), a dentifrice containing 6.5% nanoXIM•CarePaste ingredient). For that purpose, the authors subjected to microhardness testing a negative control (not subjected to any therapy), a demineralized enamel specimen and three other enamel samples, where remineralizing agents were applied in.

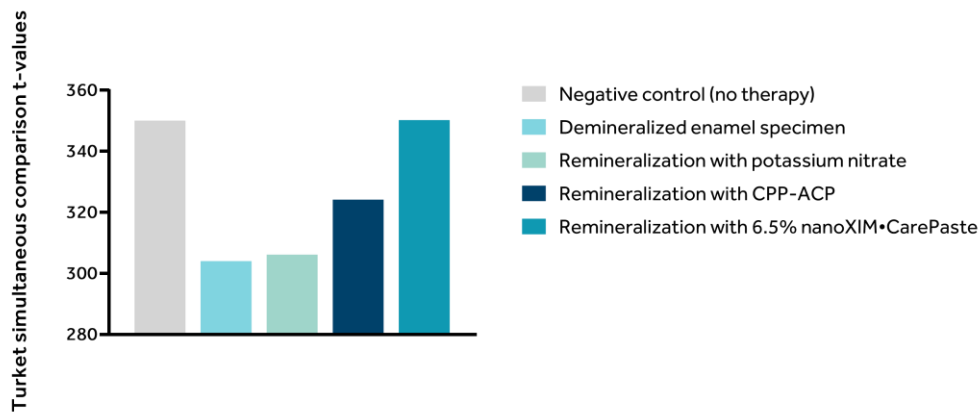


Figure 17: Comparative evaluation of surface microhardness of artificially demineralized human enamel.

- ✓ There were detected statistically significant differences in the microhardness between control and experimental samples;
- ✓ The Aclaim toothpaste containing nanoXIM•CarePaste presented the best remineralization, when compared to the other two pastes, presenting a full remineralization recovery from the demineralization initial stage.

In vitro study 6

V. Vijayasankari (2018) aimed to test the hypothesis that the remineralization potential of experimental nano-hydroxyapatite (nHAp) pastes was equally effective in comparison with commercially available pastes and control. Using scanning electron microscope with energy dispersive X-ray analysis, the present study evaluated the remineralization potential of experimental nHAp pastes and two commercial non-fluoridated remineralizing pastes: Aclaim toothpaste (Group Pharmaceuticals Ltd., India, a dentifrice containing 6.5% nanoXIM•CarePaste – corresponds to 1% nHAp) and GC tooth mousse (Recaldent™, Belgium – CG Corporation, Japan, a dentifrice containing casein phosphopeptide amorphous calcium phosphate – CPP ACP). For that purpose, the remineralization potential of experimental 1% nHAp and 10% nHAp were compared, respectively, with Aclaim's toothpaste and with CPP ACP toothpaste.

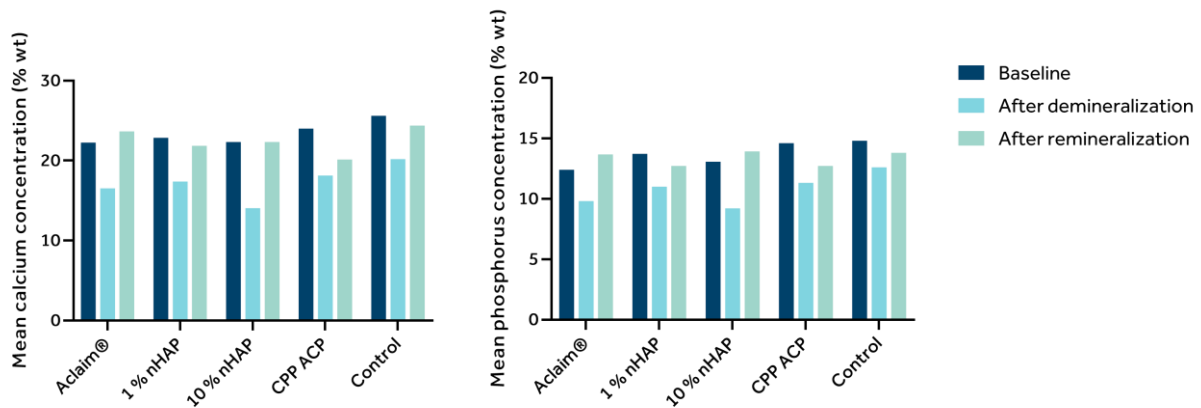


Figure 18: Comparison of mean values of calcium (left) and phosphorus (right) weight percentage at baseline, after demineralization and after remineralization in each group.

- ✓ This study found that post-remineralization calcium weight percentage was greatest in the 10% nHAp followed by the toothpaste containing nanoXIM•CarePaste (Aclaim®);
- ✓ The results revealed that the Aclaim toothpaste containing nanoXIM•CarePaste showed a significant increase in calcium and phosphorus weight percentage after remineralization;
- ✓ With just 1% nHAp content (6.5% nanoXIM•CarePaste), the Aclaim toothpaste showed superior performance to the experimental 1% nHAp paste, evidencing that not all nano-hydroxyapatite toothpastes perform the same way.

In vitro study 7

An *in-vitro* study was performed to evaluate and compare the remineralization potential of four different remineralizing agents, i.e., nano-hydroxyapatite crystals, bioactive glass, casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), and fluoride on initial enamel lesion. For that purpose, sixty human maxillary central incisors were used. Samples were randomly divided into four groups (n = 15): Group 1 – nanohydroxyapatite-containing dentifrice (Aclaim – 6.5% nanoXIM•CarePaste); Group 2 – bioactive glass containing-dentifrice (SHY-NM); Group 3 – CPP-ACP-containing dentifrice; and Group 4 – fluoride-containing dentifrice.

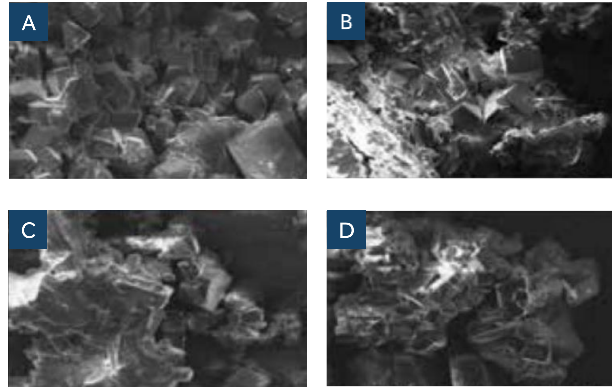


Figure 19: Scanning electron microscopic analysis after the pH cycling for 10 days, to evaluate remineralization.
A: nano-hydroxyapatite; B: bioactive glass; C: CPP-ACP; D: fluoride.

- ✓ After remineralization, there is a significant difference in mean microhardness between the groups;
- ✓ Nano-hydroxyapatite-containing dentifrice (with nanoXIM•CarePaste) has the highest remineralizing potential followed by bioactive glass, CPP-ACP, and fluoride. Therefore, fluoride has the least remineralizing potential as compared to other groups, used in the study.

Whitening

In vitro clinical study 1

The purpose of this study was to investigate the tooth-whitening effects of mouthrinses containing different sizes of hydroxyapatite (HAp) particles after prolonged application time and compare them with a commercial whitening mouthrinse. For that, fifty bovine incisors were stained and randomly distributed into five groups: the HAp groups with 3 μm , 200 nm and 50 nm particle size (nanoXIM•CarePaste), the commercial whitening mouthrinse group and the distilled water group. The teeth underwent prolonged mouthrinse applications that were equivalent to simulated three and six-month mouth rinsing applications. Tooth color was measured and calculated before and after mouth rinsing.

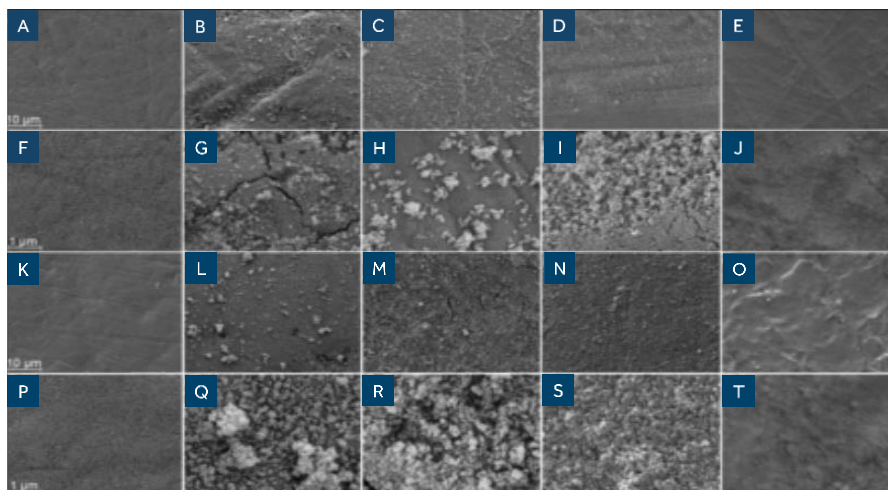


Figure 20: The mouthrinse-treated enamel surfaces were visualized at 1,000 \times and 10,000 \times after applications equivalent to three and six months.

A and F: untreated enamel surface at 1,000 \times .

K and P: untreated enamel surface at 10,000 \times .

B-E: the enamel of the 3 μm , 200 nm, 50 nm HAP groups and the commercial mouthrinse group at 1,000 \times after applications equivalent to three months.

G-J: the enamel of the 3 μm , 200 nm, 50 nm HAP groups and the commercial mouthrinse group at 10,000 \times after applications equivalent to three months.

L-O: the enamel of the 3 μm , 200 nm, 50 nm HAP groups and the commercial mouthrinse group at 1,000 \times after applications equivalent to six months.

Q-T: the enamel of the 3 μm , 200 nm, 50 nm HAP groups and the commercial mouthrinse group at 10,000 \times after applications equivalent to six months.

- ✓ The whitening effect of HAp mouthrinses after the prolonged application time was confirmed.
- ✓ The HAp mouthrinses exhibited similar tooth-whitening effects to the commercial whitening mouthrinse. It was also observed that the tooth-whitening performance of HAp was dependent on the particle size and application time;
- ✓ The HAp 50 nm particles (nanoXIM•CarePaste) showed better tooth-whitening performance after a longer period of mouth rinsing than the microsized HAp particles.

In vivo clinical study 1

In this study, it was evaluated the whitening efficacy of VITIS Whitening toothpaste (Dentaid S.L., Spain) that contains 3% of nanoXIM•CarePaste.

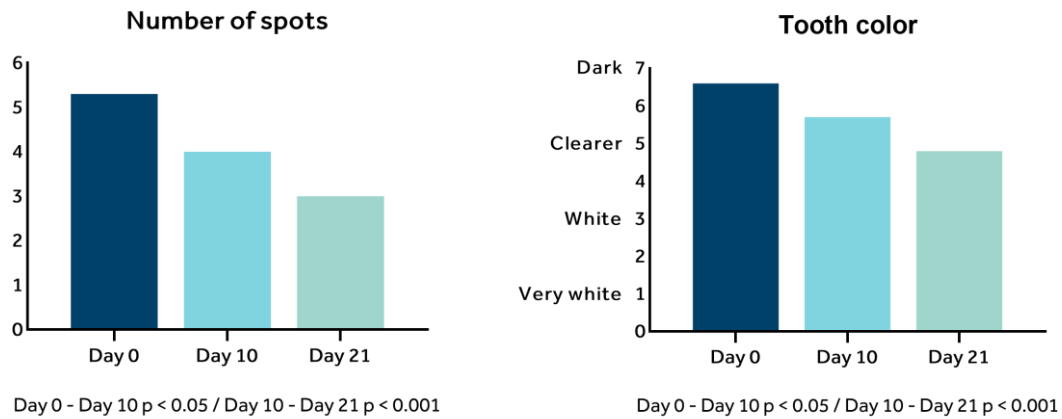


Figure 21: Whitening effect of VITIS Whitening toothpaste (containing 3% nanoXIM•CarePaste). A reduced number of dental stains and whiter teeth are achieved after ten and twenty-one days of use.

- ✓ A 24% reduction in the number of dental staining was observed in 65% of patients after ten days of use;
- ✓ A 38% reduction in the number of dental staining was observed in 75% of patients after twenty-one days of use;
- ✓ After ten days of use, it was noticed teeth whitening in 45% of patients;
- ✓ After twenty-one days of use, it was noticed teeth whitening in 75% of patients.

Conclusion

The studies stated in this document evidence the success of nanoXIM•CarePaste as an oral care ingredient. *In vitro* and clinical studies showed excellent performance in the treatment of dental hypersensitivity, with successful dentin tubule occlusion and pain relief. Moreover, the research demonstrates the ability of nanoXIM•CarePaste to repair the surface of teeth enamel and restore its natural whiteness.



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