



MI Paste™ & MI Paste Plus™

A Collection of Scientific Studies



THE USE OF MI PASTE PLUS™ IN ORTHODONTICS – A RANDOMIZED CONTROLLED TRIAL

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INTRODUCTION

Bacteria in dental plaque metabolize carbohydrates and generate organic acids as byproducts, which begin the demineralization process. The first stage of enamel demineralization involves surface softening. The second stage can be seen as dissolution in the deeper part of the enamel. Free calcium and phosphate ions diffuse from sites deep within the enamel to the tooth surface. White spot lesions (demineralization) can occur in as many as 50% of teeth with orthodontic appliances and in up to 50% of treated patients. MI Paste Plus™ has been shown in some initial case reports to be useful in the reduction of white spot lesions.

Background on MI Paste Plus

- RECALDENT™ (CPP-ACP), in MI Paste Plus™, is a complex of Casein Phosphopeptide (CPP) and Amorphous Calcium Phosphate (ACP). It binds to biofilms, plaque, bacteria, hydroxyapatite, and surrounding soft tissue.
- Under low oral pH conditions, CPP-ACP releases calcium and phosphate in a unique soluble form (CaHPO₃), which is then transported into the tooth structure and enables strengthening of enamel.

Review of Literature

- 49.6% of debonded patients showed white spot formation compared with only 24% of non-orthodontically treated controls. (Gorelick)
- Demineralization occurred in 14.5% of debonded teeth. (Banks) Casein phosphopeptides (CCP), present in MI Paste Plus™, stabilizes calcium phosphate in solution, maintaining a high-concentration gradient of calcium and phosphate ions and ion pairs which help to remineralize subsurface demineralized lesions. (Reynolds)
- Casein phosphopeptides may be used to localize Amorphous Calcium Phosphate (ACP) in dental plaque, maintaining a state of supersaturation with respect to tooth enamel, reducing demineralization and enhancing remineralization. (Rose)

MATERIALS AND METHODS

- Sixty from a possible 65 patients, who were undergoing routine orthodontic treatment, were recruited for this prospective, randomized clinical trial. All patients requiring orthodontic treatment were asked to participate in this prospective study. A double blind method of randomization was used to determine if the patient received the MI Paste Plus™ (GC America, Illinois, USA) or Tom's of Maine Toothpaste (placebo) (Salisbury, UK).
- Each patient was asked to administer the paste onto a fluoride tray for a minimum of 3-5 minutes each day at night after brushing.
- Photographic records obtained in a light controlled environment were used to record the presence or absence of white spot lesions in both sets of study groups. The Enamel Decalcification Index-EDI (Banks and Richmond) was used to determine the number of white spot lesions per surface and present at each time interval. Patients were followed at 4-week intervals for three months.
- ICDAS, which is essentially a scoring system from 0-6, was used in determining the level of caries or cavitations present. This system was also used for each tooth at each time interval.

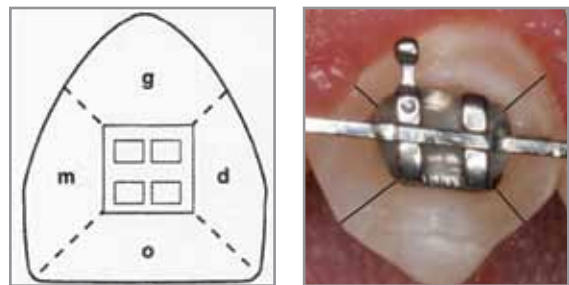


Figure 1. Enamel Decalcification Index. Facial surface of each tooth was divided into four areas. A score was allocated for each area of each tooth: 0=No decalcification to 3=Decalcifications covering 100% of the area.

RESULTS

- 50 patients (26 MI Paste Plus™ and 24 Placebo Paste) completed the study.
- The EDI scores for all surfaces were 271 and 135 at the start of treatment and 126 and 258 at the end of treatment for the MI Paste Plus™ and placebo paste groups respectively.
- The EDI scores in the MI Paste Plus™ group reduced by 53.5% while the placebo group increased by 91.1% during the study period.
- A three-way ANOVA was done for the average EDI scores. Fisher's PLSD Intervals were used to compare mean EDI scores. The surface type, the product/time interactions, and the product/surface interactions of the mean EDI scores proved significant ($p < 0.05$).
- Two-way ANOVA was used to analyze ICDAS scores. As average EDI scores slowly decreased for the MI Paste, so did the ICDAS scores. Likewise, as average EDI scores slowly increased for the placebo, so did the ICDAS scores.

RESULTS (CONT.)

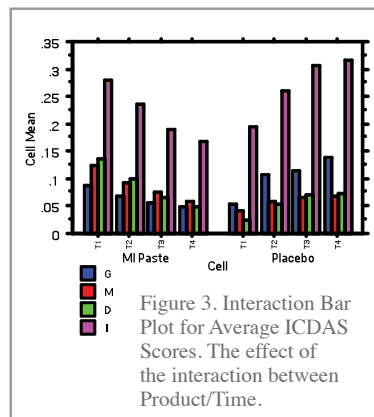
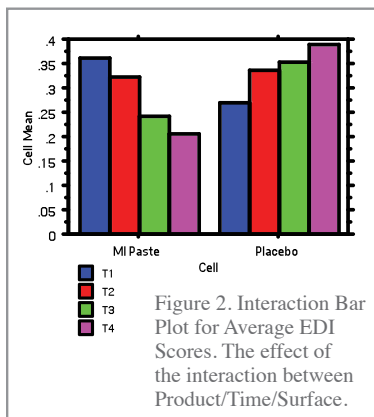


Figure 4. Right buccal intraoral photographs of patient at T1 to T4 using MI Paste Plus™.

DISCUSSION

The two products did not behave the same over time. The MI Paste Plus™ EDI scores for each surface decreased for each time period while the placebo's increased.

- There seemed to be a strong correlation with EDI and ICDAS scores.
- The effect of surface on mean EDI scores is highly significant. The distal surface in the MI Paste Plus™ group showed the greatest percent decrease in decalcifications, and in the placebo group, the distal and gingival surfaces showed the greatest percent increase in white spot formation.
- For MI Paste Plus™ and the placebo, at every time point, the incisal edge average EDIs differed significantly with each of the other surfaces. This showed a tendency, in this patient population, for incisal decalcifications, even though it is reported that the gingival quadrant is most susceptible to white spots. In this study, systematic error was unlikely, as the results were independently obtained from two operators and intra-operator reliability was high.
- It is also shown that after T1 the gingival surfaces of the MI Paste Plus™ sample had less mean EDI scores than the gingival surfaces of the placebo. This result suggests that the gingival portion of the tooth is particularly sensitive to orthodontic treatment during white spot lesion formation especially in the placebo group.
- One limitation of this study is that the compliance of the patient could not be controlled, standardized, or measured.
- In addition, no standard delivery system of MI Paste Plus™ existed previously, so the protocol of using the trays for 3-5 minutes per night was developed and chosen on the basis of best clinical practice.

CONCLUSIONS

The null hypothesis that there was no difference between MI Paste Plus™ and the placebo in their effects on the formation and resolution of white spot lesions for patients undergoing orthodontic treatment was rejected.

- MI Paste Plus™ not only had a preventive action of white spot development during orthodontic treatment, but also decreased the number of white spot lesions present.
- The placebo had no preventive action on white spot development during orthodontic treatment; the number of lesions actually increased.
- MI Paste Plus™ had an impact on reducing white spots on the gingival surface, whereas the placebo group had the opposite effect.
- The incisal surface effect on mean EDI scores over time and between products was highly significant in that the incisal EDI scores were consistently higher than that of each of the other surfaces (mesial, distal, gingival).



Figure 5. Intraoral photographs of teeth #s 6, 7, 8 of patient at T1 and T4 using the placebo.



Figure 6. Intraoral photographs of tooth # 8 of patient at T1 and T4 using MI Paste Plus™.

WATER SOLUBLE CALCIUM, PHOSPHATE AND FLUORIDE OF VARIOUS DENTAL PRODUCTS

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ABSTRACT

Introduction:

Various dental products containing calcium phosphate and/or fluoride on the market have claims of remineralization of dental hard tissue. Most of these claims have not been substantiated in clinical trials. The ability to provide water soluble calcium phosphate and fluoride is proposed to be a surrogate measure of the remineralization potential of these products.

Objectives:

The aim of this study was to compare the water soluble calcium phosphate and/or fluoride levels of 21 commercially available dental products with added calcium.

Methods:

Three batches of each product were obtained and each batch was analyzed in triplicate. One gram was added to 19mL of distilled water and the slurry mixed overnight on a rotating platform. The slurry was then centrifuged at 16,000g for ten minutes at room temperature, and 1mL of the supernatant (water soluble) was collected for analysis. Total and water soluble samples were diluted with distilled water, acidified with HNO and analyzed using a Dionex ICS3000.3.

Results:

Fluoride in the analyzed dental products was mostly water soluble. Calcium in the products was found to have low water solubility except for MI Paste Plus™, which contained 321.8 ± 2.6 μmol water soluble calcium per gram of crème (14 times or more over that of the other products). MI Paste Plus™ also contained the highest amount of water soluble phosphate (245.7 ± 2.7 μmol/g). The high water solubility of the calcium, phosphate and fluoride in MI Paste Plus™ was attributed to the presence of the casein phosphopeptides.

Conclusion:

MI Paste Plus™ was shown to contain highly water-soluble calcium, phosphate and fluoride which would be available for remineralization of dental hard tissue.

INTRODUCTION

Dental caries is initiated by organic acid produced by cariogenic bacteria of dental plaque, resulting in the demineralisation of dental hard tissue. The management of early caries lesions by remineralization has been recommended by Tyas MJ et al. (2000). The ability of dental products to provide water soluble calcium phosphate and fluoride ions is proposed to be a surrogate measure of the potential of remineralization (Reynolds EC, 2008). Various dental products containing calcium, phosphate and fluoride on the market have claims of remineralization of dental hard tissue. Most of these claims have not been substantiated in clinical trials. The active ingredients of the commercial products, their recommended usage, and the claims are listed alphabetically in Table 1. The aim of this study was to determine the water soluble calcium, phosphate and fluoride ions levels of these products.

Active Calcium Ingredient	Products	Usage	Claims and Mechanisms
Amorphous Calcium Phosphate (ACP)	Age Defying Toothpaste Relief ACP Day White ACP Nite White ACP Whitening Booster Enamel Pro	Homecare toothpaste Home desensitising gel Home bleaching gel Prophylaxis paste	Combine soluble salts of calcium and phosphorous to form unstabilised ACP to: • Reduces Sensitivity • Rebuilds Enamel • Helps Reduce Caries • Improves Luster
Medical Hydroxyapatite (Nano mHAP)	Apagard M-plus Apagard Premio Apagard Smokin	Homecare toothpaste	Nano-mHAP particle to: • Effectively remove plaque (no abrasive) • Repair microscopic enamel fissure • Remineralise incipient caries
Sodium Calcium Phosphosilicate (NovaMin®)	Dr. Collins Oravive® Renew SootheRx® DenShield™ NuCare®	Homecare toothpaste Home desensitising paste Prophylaxis Paste	Rapid release of sodium, calcium and phosphorous when contact with water to: • Occlude dentinal tubule and desensitize • Remineralise tooth surface
Casein phospho-Peptide Stabilised amorphous calcium phosphate (Recaldent®)	Tooth Mousse Plus	Home desensitising paste	Bioactive ACP combined with fluoride to: • Strengthen enamel • Buffer plaque pH • Remineralise incipient caries lesion • Occlude dentinal tubules and desensitize • Reduce erosion
Arginine, calcium and cariostatic anion (Sensistar®/CaviStat®)	DenClude ProClude	Home desensitising paste Prophylaxis Paste	Arginine and calcium from the complex: • Reduce cariogenicity of plaque • Neutralise and maintain plaque pH • Reduce solubility of dental hard tissue • Enhance remineralisation of dental hard tissue • Form insoluble complex occlude dentinal tubules
Functionalised Tri-calcium phosphate (fTCP)	Clinpro 950 Clinpro 5000	Homecare toothpaste	fTCP combine with fluoride to: • Effectively remove plaque (low abrasive) • Strengthen teeth • Remineralise incipient caries

MATERIAL AND METHOD

In total, three batches of each of the 21 products were obtained and each batch was analyzed in triplicate. One gram of each paste was added to 19mL of distilled water in a 50mL centrifuge tube. The slurry was mixed overnight on a rotary suspension mixer (RSM6 Ratek Instrument, VIC, Australia) at a speed of approximately 20rpm. One mL of mixed slurry (total) was collected for analysis. The remaining slurry was then centrifuged at 16,000g for 10min at room temperature (Avanti J-25I Beckman Coulter, CA, USA). One mL of the supernatant (water soluble) was collected for analysis. Total and water soluble samples were diluted with distilled water, acidified with 0.01M of HNO (Merck, Germany), thoroughly three mixed and transferred into a 10mL syringe fitted with a 0.2mm filter (Minisart, Sartorius VIC, Australia). Filtrates were injected into a labelled Dionex sampling vial (Dionex Corporation, CA, USA). Levels of inorganic ions were determined using an automatic ion chromatography system, equipped with two columns for both cation (IonPac CS12) and anion (Ion Pac AS18), and two separated conductivity detector (ICS3000, Dionex Corporation, CA USA). A combined seven anion standard (#56933) and a combined six cation standard (#046070) were diluted 20, 50 and 100 times with distilled water to calibrate and quantify the conductivity reading.

RESULTS

Fluoride in the 21 dental products was mostly water soluble and mostly matched the claimed amount (Fig.1), although some products containing ACP (Age Defying toothpaste) or Novamin (NuCare prophylaxis paste) did exhibit low fluoride recoveries. Nano-mHAP and Sensistat products and one of the Novamin products (NuCare prophylaxis paste) contained large amounts of added calcium. However, most of this added calcium was insoluble in water, hence unavailable (Fig. 2). MI Paste Plus™ was shown to contain $321.8 \pm 2.6 \mu\text{mol}$ water soluble calcium per gram of crème (14 times or more over that of the other products (Fig. 2)). MI Paste Plus™ was also shown to have the highest amount ($245.7 \pm 2.7 \mu\text{mol/g}$) of water soluble phosphate for all products analyzed (Fig. 3)

Fig. 1

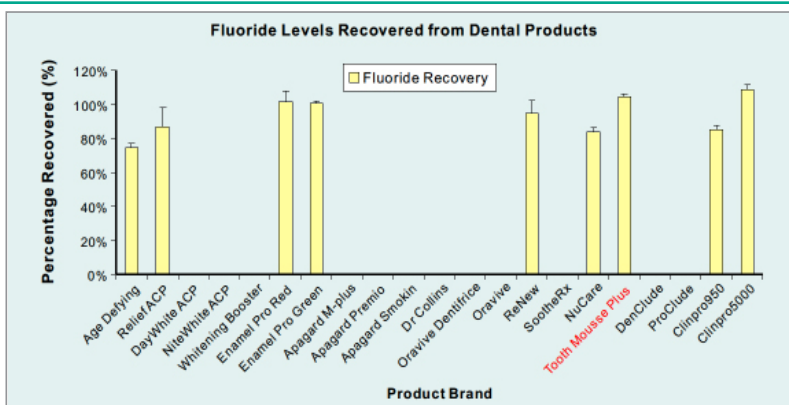


Fig. 2

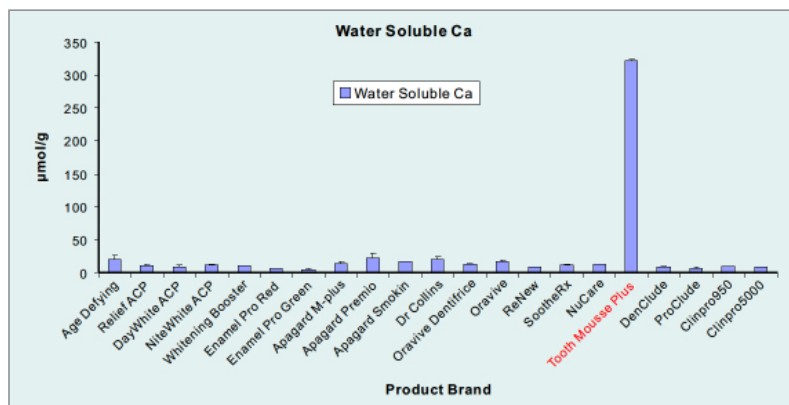
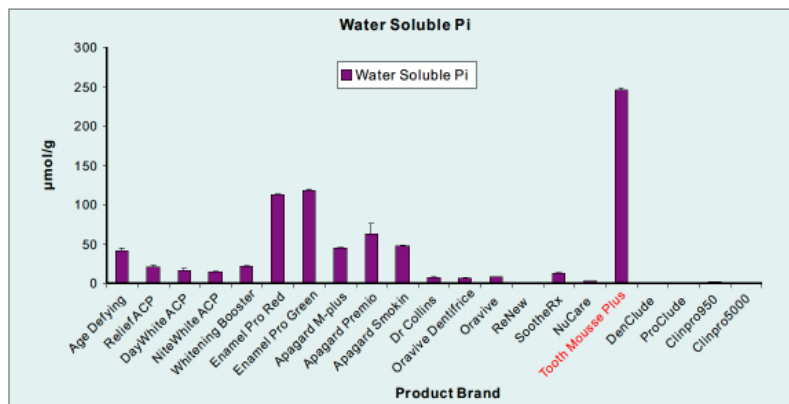


Fig. 3



DISCUSSION

Of all 21 products, only MI Paste Plus™ containing casein phosphopeptide (CPP), exhibited high levels of water soluble calcium, phosphate and fluoride ions. These high levels of water soluble ions were attributed to the presence of the CPP in CPP-ACP (RECALDENT™). These high levels of water soluble calcium, phosphate and fluoride ions are consistent with the recent clinical trials of Tooth Mousse and CPP-ACP / fluoride toothpastes showing enhanced remineralization of caries lesions (Reynold EC et, al., 2008, Bailey DL et, al., 2009). ACP products contained a much lower level of water soluble calcium, phosphate and/or fluoride. This may be attributable to the unstable nature of ACP, which precipitates rapidly upon mixing. Age Defying toothpaste was not a dual chamber design like the other ACP products. This may further reduce the availability of water soluble ions in the product. The other products containing nano mHAP, Novamin, Sensistat and fTCP as a source of calcium ions also exhibited very poor water soluble calcium levels. This could be attributed to the very low solubility of the form of calcium used in the products.

CONCLUSION

MI Paste Plus™ was shown to contain highly water-soluble calcium, phosphate and fluoride which would be available for remineralization of dental hard tissue.

COMPARISON OF TOOTH MOUSSE PLUS™ (MI PASTE PLUS™) WITH CLINPRO IN SITU

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ABSTRACT

Introduction:

Two dental products [Tooth Mousse Plus™/MI Paste Plus™ (TMP) and Clinpro™† (CP)] containing calcium, phosphate and fluoride are claimed to enhance enamel remineralization over fluoride products.

Objectives:

To compare remineralization of enamel subsurface lesions by TMP, CP, 1000 ppm F and 5000 ppm F in a double-blind, randomized, cross-over in situ study.

Methods:

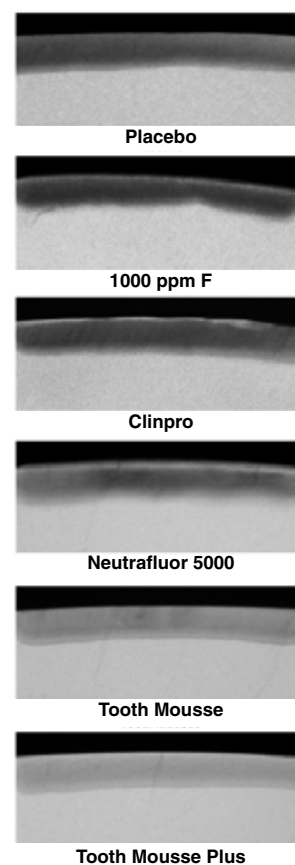
Human enamel specimens with subsurface lesions were prepared and inserted into intra-oral appliances worn by healthy volunteers (n=6). A slurry (1g paste in 4mL H₂O) of each paste was rinsed for 60 sec, 4 times per day for 10 days. Six pastes were tested (i) placebo, (ii) 1000 ppm F, (iii) 5000 ppm F, (iv) Tooth Mousse™/MI Paste™ (TM), (v) TM plus 900 ppm F (TMP) and (vi) Clinpro™† with 1000 ppm F (CP). Pastes were randomly assigned and each subject crossed over to each paste after a day washout period. Calcium, inorganic phosphate and fluoride levels were measured in post-rinse/saliva samples using ion chromatography. Mineral content was measured using transverse microradiography.

Results:

Only TM and TMP significantly increased salivary calcium and phosphate levels, with TMP increasing salivary calcium, inorganic phosphate and fluoride levels to 51.6 ± 15.7 mM, 35.4 ± 10.3 mM and 108.3 ± 38.1 ppm F respectively. The pastes produced the following levels of remineralization of the enamel subsurface lesions: Placebo $3.7 \pm 2.1\%$; 1000 F $7.9 \pm 2.1\%$; Clinpro™† $9.6 \pm 0.9\%$; 5000 F 16.3 ± 1.3 ; TM 24.2 ± 2.3 and TMP $29.3 \pm 0.7\%$. Clinpro™† was not significantly different to 1000 ppm F whereas TM and TMP were superior to 5000 ppm F with TMP producing the highest level of enamel lesion remineralization.

Conclusion:

TMP containing casein phosphopeptide-stabilized calcium, phosphate and fluoride ions was superior to functionalized TCP and F of Clinpro™† in remineralization of enamel subsurface lesions in situ.



NEW APPROACHES TO ENHANCED REMINERALIZATION OF TOOTH ENAMEL

NJ. COCHRANE F. CAI, NL. HUQ, MF. BURROW, EC. REYNOLDS.

Dental caries is a highly prevalent diet-related disease and is a major public health problem. A goal of modern dentistry is to manage non-cavitated caries lesions non-invasively through remineralization in an attempt to prevent disease progression and improve aesthetics, strength, and function. Remineralization is defined as the process whereby calcium and phosphate ions are supplied from a source external to the tooth to promote ion deposition into crystal voids in demineralized enamel, to produce net mineral gain. Recently, a range of novel calcium-phosphate-based remineralization delivery systems has been developed for clinical application. These delivery systems include crystalline, unstabilized amorphous, or stabilized amorphous formulations of calcium phosphate. These systems are reviewed, and the technology with the most scientific evidence to support its clinical use is the remineralizing system utilizing casein phosphopeptides to stabilize and deliver bioavailable calcium, phosphate, and fluoride ions. The recent clinical evidence for this technology is presented and the mechanism of action discussed. Biomimetic approaches to stabilization of bioavailable calcium, phosphate, and fluoride ions and the localization of these ions to non-cavitated caries lesions for controlled remineralization show promise for the non-invasive management of dental caries.

New Approaches to Enhanced Remineralization of Tooth Enamel. NJ. Cochrane F. Cai, NL. Huq, MF. Burrow, EC. Reynolds, *J Dent Res* 89(Spec Iss B):11, 2010 (www.dentalresearch.org).

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MI Paste Plus™
is like vitamins
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- Quickly stops sensitivity
- Helps strengthen your teeth to aid in keeping them cavity resistant
- Calcium, phosphate and fluoride in nature's correct ratio



LATEST TECHNOLOGY IN KEEPING YOUR TEETH STRONG AND HEALTHY!

MI Paste Plus is the only dental product with RECALDENT™ (CPP-ACP) that contains a naturally occurring, milk-derived protein. It is the ONLY calcium, phosphate and fluoride supplement available that can help re-deposit those essential strengthening minerals back into your teeth. MI Paste Plus is not a toothpaste — it is a topical tooth crème that can be used safely several times daily at home. It helps to keep your smile strong and healthy for a lifetime!

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