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Clinical Trial of CPP-ACP in Sugar-Free Chewing Gum

In one of the largest oral health clinical trials conducted in Australia, 2,720 students chewed sugar-free gum three times a day for two years.

The study found that subjects who chewed gum containing the calcium phosphate complex CPP-ACP (casein phosphopeptide-amorphous calcium phosphate) had significantly lower rates of dental decay progression on approximal surfaces than those who chewed a standard sugar-free gum.

Clinical trial of CPP-ACP in **sugar-free chewing gum** conducted by the Cooperative Research Centre for Oral Health Science at The University of Melbourne. A comprehensive article on this clinical trial appears in the journal *Caries Research*, 42:171-184 (2008) by MV Morgan, GG Adams, DL Bailey, CE Tsao, SL Fischman, EC Reynolds.



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Background

The CPP-ACP (casein phosphopeptide-amorphous calcium phosphate) complex was developed by Professor Eric Reynolds and his research team in the School of Dental Science at The University of Melbourne. The complex is derived from peptides isolated from the milk protein casein, complexed with calcium and phosphate, and has been found to be effective at replacing lost minerals – or remineralizing – decay-damaged teeth.

In a number of controlled trials, sugar-free gum without CPP-ACP has been found to have a decay preventive effect, when compared with not chewing gum at all.

This trial sought to measure any caries (dental decay) preventive effect of chewing sugar-free gum containing the CPP-ACP complex, when compared to a standard sugar-free chewing gum.

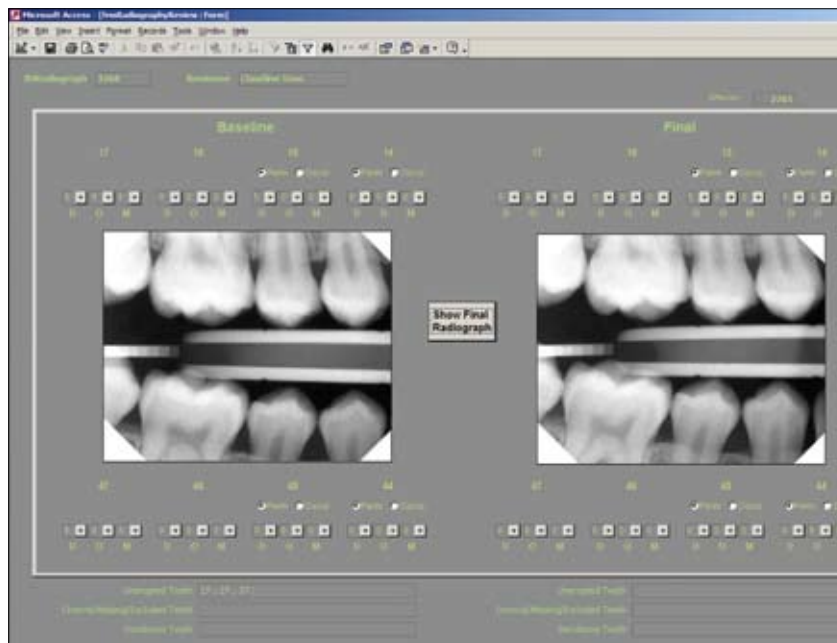
Study sample

The study was a double-blind randomized controlled trial of 2,720 year 7 students, with an average age of 12.7 years, attending 29 secondary schools in the metropolitan area of Melbourne.

All students in the sample were living in an area with a water supply fluoridated at approximately 1.0ppm. They were also all provided with a standard fluoride toothpaste for normal brushing at home. Any difference measured in caries progression or regression would be over and above the effect of this regular fluoride intake.

Within each school, participating students were divided into two groups: half the students were randomly allocated the gum containing CPP-ACP and the other half the control sugar-free chewing gum. Both gums were identical in appearance, taste and smell. The students, the clinical examiners and those involved in distributing the test products were not aware of which chewing gum had been randomly assigned to each student.

Subjects were excluded from the study if they had milk protein allergies, phenylketonuria, or regularly used antibiotics or medications that affect salivary flow rates.



A custom-designed database provided a split-screen interface to allow radiographic image reading and data entry.

Test products

Control subjects chewed a standard sorbitol-based sugar-free gum, while intervention subjects chewed an identical gum containing 3% w/w CPP-ACP.

All subjects were requested to chew their gum three times a day throughout the two-year study for 10 minutes each time.

Measurement

The progression or regression of caries over the course of the study was measured by dentists using visual-tactile examinations and digital bitewing radiographs.

Subjects received a visual-tactile examination at baseline, 12 months and 24 months. Bitewing radiographs of the posterior teeth were taken at baseline and at 24 months.

A purpose-built mobile dental van allowed radiographs to be taken on site at the schools. A custom-designed rigid aiming device was used for the radiographs to enable maximum standardization of images.

All radiographic images were examined and scored by a single dentist in a dedicated room with controlled light level and monitor settings. Approximal surfaces were assessed for both enamel and dentine caries. The depth of the radiolucency was measured at four levels with both the width of the enamel and the width of the dentine being subdivided.

Thirty complete sets of radiographs (baseline and 24-month) were assessed three times at random intervals for the determination of intra-examiner variability. Excellent agreement was found, with the scores assigned for extent of penetration of the caries lesion being in agreement for greater than 97.7% of surfaces. The discrepancy was greater than one depth code for less than 1% of surfaces. The intra-examiner kappa scores between the three scorings were at least 0.92.

For subjects chewing the CPP-ACP gum, the odds of a tooth surface experiencing caries progression were 18% less than for subjects chewing the standard sugar-free gum.

Following the reading and coding of the baseline and 24-month radiographs, a transition matrix, based on differences in the extent of penetration of the radiolucency, was used to score changes at the surface level. Regression of carious lesions was allowed for in that the appropriate negative scores were given when transitions to less severe grades of lesion occurred.

The statistical analysis compared the distributions of transition scores between the two gum groups using an ordinal logistic regression model.

Results

Subjects chewing the CPP-ACP sugar-free gum demonstrated a statistically significant difference in radiographically diagnosed approximal carious lesions compared with those chewing the control sugar-free gum.

The trial found that not only did the CPP-ACP group have a smaller number of tooth surfaces in which caries lesions had progressed over the two years, but this group also had a greater number of lesions that had regressed – or remineralized. The regressions involved predominantly remineralization of enamel lesions, but also a small number of dentine lesions.

Conclusions

The trial results found that chewing CPP-ACP gum provided an increased preventive effect beyond that achieved through good, basic oral care habits and chewing sugar-free gum.

The results confirm the findings of short-term *in situ* remineralization studies, and demonstrate the long-term outcomes of regular exposure of teeth to the CPP-ACP complex.

The conclusion of the clinical trial was that chewing sugar-free gum containing CPP-ACP can be regarded as an additional caries prevention tool, over and above other accepted preventive strategies such as water fluoridation and the use of fluoridated toothpaste.

Glossary

Approximal	The tooth surface between adjacent teeth
Bitewing radiography	An intraoral dental x-ray, especially useful in detecting approximal caries
Caries	Tooth decay
Carious lesion	The softening of teeth surfaces and eventual cavitation by the action of bacteria
CPP-ACP	The casein phosphopeptide-amorphous calcium phosphate complex
Dentine	The part of the tooth beneath the enamel and surrounding the pulp chamber and root canals
<i>In-situ</i> studies	Studies conducted on samples of human tissue that have been placed in another human
Radiolucency	The degree to which the tooth is able to be penetrated by x-rays. The radiolucency of lesions increases as mineral levels decline. Radiolucent areas appear black on exposed X-ray film.

Acknowledgements

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Journal article

MV Morgan, GG Adams, DL Bailey, CE Tsao, SL Fischman, EC Reynolds. The Anticariogenic Effect of Sugar-Free Gum Containing CPP-ACP Nanocomplexes on Approximal Caries Determined Using Digital Bitewing Radiography in *Caries Research*, 42:171-184 (2008).



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The Cooperative Research Centre for Oral Health Science brings together scientists, dentists, population health experts and manufacturers to find new and efficient ways of reducing the burden of oral disease in Australia and internationally.

