

**Clinical Evaluation of Chemo-Mechanical Caries Removal using Papain-based Enzyme Versus Rotary preparation in adult patients treated with partial caries removal: Randomized Clinical Trial**

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**Abstract**

The aim of the study was to evaluate the effect of caries excavation using the papain-based chemo-mechanical method (Brix 3000) versus the conventional rotary tools on the reduction of Streptococcus Mutans count, post-operative pain and patient satisfaction in occlusal carious cavities treated with partial caries removal. Forty-six permanent molars from 23 patients aged between 18 and 40 years were selected. The molars were randomly divided in a split mouth design into two groups of 23 teeth each; Group A treated with Brix 3000 method, while group B treated with conventional rotary burs. Dentin samples were collected from the patients before and after the infected caries removal, and the bacterial count was calculated. The patient satisfaction about the treatment and the post-operative hypersensitivity were recorded after 24 hours and 7 days. There was no statistically significant difference in the mean CFU/ml after both techniques brix 3000  $104.1 \pm 43.0$  and rotary  $119.1 \pm 49.9$  where

( $p=0.265$ ). However, Brix 3000 showed a statistically significant lower pain scores compared to the rotary group, both after 24 hours ( $p=0.001$ ) and after 7 days ( $p=0.003$ ). Also, Brix 3000 showed a significantly better patient perception ( $p=0.004$ ). Brix 3000 is a viable option for the minimally invasive removal of dental carious tissue, obtaining significant reductions in total bacterial count with the same effectiveness as the conventional caries removal method as well as better acceptance by the patients.

**Keywords:** Brix 3000, chemo-mechanical caries removal, bacterial reduction and post-operative pain.

**Introduction**

Dental caries is one of the most prevalent oral diseases of public oral health concern. It forms through a complex interaction over time between acid-producing bacteria, fermentable carbohydrate and many host factors including teeth and saliva.

Carious dentin consists of two distinct layers having different ultramicroscopic and chemical structures. The superficial layer (infected dentin) is highly decalcified and infected with bacteria and should thus be removed. Despite the possible discoloration, the inner layer (affected dentin) has to be preserved, since it retains the cross-banded ultrastructure of its collagen matrix and no bacterial invasion. Moreover, it is more resistant to the proteolytic attack and the progression of carious lesions (1).

Chemo-mechanical caries removal (CMCR) has been developed to overcome the shortcomings of the conventional caries removal techniques. It is a non-invasive excavation method which uses a chemical gel that selectively removes the infected dentin where collagen is degraded, maintaining the demineralized portion that is capable of being re-mineralized (2).

One of these CMCR products is the papain-base Brix 3000. Its exclusive Encapsulating Buffer Emulsifier (EBE) technology claims it has effective and selective proteolytic action to remove collagen fiber in the carious tissue (3).

The purpose of the study was to evaluate the effect of caries excavation using the papainbased chemo-mechanical method (Brix 3000) versus the conventional rotary tools on the reduction of Streptococcus Mutans count, post-operative pain and patient satisfaction in occlusal carious cavities treated with partial caries removal.

## Materials and Methods

### Study design and Eligibility criteria

This study is a double-blinded, two-armed, split-mouth and randomized clinical trial. It was conducted in the Clinic of Conservative Dentistry Department, Faculty of Dentistry, Cairo University, Egypt. A total of twenty-three participants between age 18-40 years, with good oral

hygiene who approved the trial were examined according to sample size calculation for the presence of at least two carious molars in each patient resulting in a total of forty-six carious molars.

### The teeth eligibility criteria

Simple occlusal carious molars were selected to be cavitated showing brown and softened dentin (reaching  $>1/2$  of the dentin in the radiographic examination) (4).

### Sample size calculation

Based on the previous paper by *Modimi et al., 2016* if the true difference in bacterial count between the two groups is  $0.0014 \pm 0.0015$  CFU/ml, we needed to study 19 sample in each group to be able to reject the null hypothesis. This number had to be increased to 23 in each group to compensate for possible losses during follow up. The power is 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05.

### Random Sequence generation

Randomization was done per patient using coin tossing to identify which contralateral tooth to be treated by Brix 3000 and which to be assigned to the conventional rotary technique.

### Allocation concealment mechanism

Individual opaque sealed envelopes were used to conceal the randomization sequence according to the treatment groups; A or B and the side; R or L, which were coded as RA, LB, RB or LA. Envelopes were allocated by another participant who was not involved in any of the phases of the clinical trial.

### Blinding

Blinding of the operator was not possible. However, the participant who was responsible for; the dentin samples collection, the postoperative pain and patient satisfaction assessment was blinded from the followed excavation protocol. Also, the microbiologist and the statistician were blinded from the tested variable.

### **Initial cavity preparation**

All the cavities were prepared under local anesthesia and rubber dam isolation.

### **Baseline dentin sample collection**

In both groups, the central cariogenic biomass and superficial parts of the necrotic dentin were removed with the excavator and then discarded. Then, a dentin sample was collected using a sharp, sterile excavator (Maillefer, Dentsply, Switzerland). The dentin samples were immediately transferred to a sterile disposable test tube. It contained a 1.5 ml thioglycollate medium used as a carrier and kept in an icebox to be transferred to the microbiology laboratory for processing within two hours (3).

### **Removal of the remaining carious infected dentin**

In the (Brix 3000) group; the gel was applied with a blunt spoon excavator and left for 2 minutes, the Brix gel starts clear, and then it turns turbid because of the decomposition of the carious lesion. The softened dentin was then scraped away using a blunt excavator in a pendulum movement without pressure (3,5).

For the conventional rotary technique: a high-speed hand piece (T3 mini, Sirona GmbH, Bensheim, Germany) was used under air/water coolant to remove the carious lesion beyond dentin/enamel junction, using conventional 330 burs (Dentsply Midwest Type 385261) and round bur of low speed (5).

### **Checking for the excavation endpoint**

Seek-caries detector dye was applied to the prepared cavities to standardize the caries removal endpoint in both groups (6).

### **Post-operative dentin sample collection**

In both groups: a second dentin sample was collected after caries removal and transferred to microbiology laboratory for processing within two hours (7,8).

### **Restorative treatment**

All the cavities were restored using Equia Forte restorative material. All the materials' specifications, compositions, manufacturers and lot numbers are presented in table 1.

### **Microbiological Analysis**

The number of bacteria obtained for a given amount of dentin was used to estimate the number of bacteria present in 1 mg of dentin (CFU/mg) (9,10,11).

### **Post-operative pain assessment**

Every patient was asked to rate his pain perception for every side on a 10 point visual analogue scale 24 hours and 7 days after the treatment. The scale was divided into 5 parts: 0 = no pain, 1-3 = mild pain, 4-6 = moderate pain, 7-9 = severe pain and 10 = extreme pain (12).

### **Patient satisfaction assessment**

Every patient was asked several questions just after the treatment related to the degree of satisfaction about each treatment regarding the time, the discomfort and the overall stress of every treatment. The feedbacks were reported through a scale from 0 (extreme satisfaction) to 10 (extreme un-satisfaction).

### **Statistical analysis**

Data were statistically described in terms of mean  $\pm$  standard deviation (SD). Comparison between the study groups was done using Mann Whitney U test for independent samples. Within group comparison was done using Wilcoxon signed rank test for paired (matched) samples. The categorical data were explored for normality using Kolmogorov-Smirnov and Shapiro-Wilk tests.

All statistical calculations were done using computer program IBM SPSS (Statistical

Package for the Social Science; IBM Corp, Armonk, NY, USA) release 22 for Microsoft Windows.

Table 1: Materials' specifications, compositions, manufacturers and lot numbers:

Material	Specification	Composition	Manufacturer	Lot no.
Brix3000	Papain-based chemomechanical caries removal agent	Papain (3,000 U/mg in a concentration of 10%), a protein extracted from papayain which the papain is bio-encapsulated by using EBE Technology, a proteolytic enzyme obtained from leaves latex and fruits of green papaya (Carica Papaya)	Brix SRL Medical Science, Argentine	412352
Sable Seek	Caries detector dye	Food, drug and cosmetic dyes in an aqueous glycol base	Ultradent Products, Inc., South Jordan, Utah 84095 USA	BDVP2
MitisSalivarius Agar	Mitis-Salivarius Agar	Casein enzymic hydrolysate 15.00 gm/L Peptic digest of animal tissue 5.00 gm/L Dextrose 1.00 gm/L Sucrose 50.00 gm/L Dipotassium phosphate 4.00 gm/L Trypan blue 0.075 gm/L Crystal violet 0.0008 gm/L Agar 15.00 gm/L.	HiMedia Laboratories Pvt.Ltd, LBS Marg, Mumbai - 400086, India	0000288211
Thioglycollate medium	Thioglycollate medium	L-cystine 0.5 gm/L Sodium chloride 2.5 gm/L Glucose 5.5 gm/L Yeast extract 5.0 gm/L Pancreatic digest of casein 15.0 gm/L Sodium thioglycolate 0.5 gm/L/L	Oxoid Ltd. Wade Road Basingstoke, Hants, UK	952625
Cavity conditioner	Cavity cleaning agent	20% polyacrylic acid solution	GC Corporation, Tokyo, Japan	41131902
EQUIA® Forte	Bulk-fill, self-curing restoration	Powder: 95% strontium fluoroaluminosilicate glass, 5% polyacrylic acid Liquid: 40% aqueous polyacrylic acid	GC Corporation, Tokyo, Japan	1502249

	Self-adhesive lightcured resin coating.	Multifunctional urethane methacrylate, methyl methacrylate, silicone dioxide (nanofiller), and phosphoric ester monomer (adhesive monomer)	GC	3020021
<b>EQUIA® Forte Coat</b>			Corporation, Tokyo, Japan )	

**Results**

**a. The bacterial count**

There was no statistically significant difference in the mean CFU/ml after both techniques brix 3000 104.1 ±

43.0 and rotary 119.1 ± 49.9 where (p=0.265). However, the chemo-mechanical caries removal Brix 3000 exhibited a more percentage reduction in bacteria count compared with the rotary group (Table 2).

Table (2): Mean and SD of values before and after in brix and rotary

Bacterial count CFU/ml	Brix (n = 23)	Rotary (n = 23)	p value
Value before (mean ± SD)	230.2 ± 76.1	246.5 ± 50.9	0.634 (NS)
Value after (mean ± SD)	104.1 ± 43.0	119.1 ± 49.9	0.265 (NS)
Percentage reduction	54.6%	51.5%	
P-value	>0.05		

**b. The post-operative hypersensitivity**

Brix 3000 showed a statistically significant lower pain scores compared to the rotary group, both after 24 hours (p=0.001) and after 7 days (p=0.003) (Table 3).

Table (3): The mean, standard deviation (SD) values of post-operative pain of the two groups at 24 hours and 7 days.

Variables	Hypersensitivity				
	Brix3000		Rotary		p-value
	Mean	SD	Mean	SD	
After 24hrs	1.739	1.356	3.522	1.648	0.001*
After 7 days	0.609	0.783	1.609	1.234	0.003*
p-value	0.002*		<0.001*		

\*; Significant (p<0.05)

**c. Patient satisfaction results**

Brix 3000 showed a statistically significant better satisfaction scores compared to the rotary group, where ( $p=0.004$ ) Table (4).

Table 4: The mean, standard deviation (SD) values of patient satisfaction between the two groups.

Variables	Satisfaction	
	Mean	SD
Brix3000	0.913	0.900
Rotary	2.304	1.690
<i>p-value</i>	0.004*	

**Discussion**

Dental caries is a complex, continuous, dynamic, biologic process consisting of periods of progression alternating with periods of arrest or even partial repair. The principle aim of cavity preparation is to eliminate all infected dentin caries to prevent the progression of carious processes and to provide a sound structural base for restoration (13).

Over the decades, tremendous efforts were done to study the management of deep dental caries. Traditionally, caries was removed mechanically with hand excavators and rotary instruments. These procedures have many limitations as they may cause overextension of cavities and healthy tissue removal leading to weakening of the remaining tooth structure. Also, increasing the risk of postoperative pulpal symptoms and pulp exposure due to excessive pressure, vibration and heat generation (14).

Partial caries removal protocol was followed in the treatment of all carious lesions. As a number of studies found mechanical removal unable to fully eliminate all bacteria from a cavity, partial removal to soft dentine reduces the risk of pulpal exposure significantly as compared with complete removal to hard or selective removal to firm dentine. Based on the understanding of caries, removing bacteria does not seem a necessity before placing a restoration, as any restoration that seals the preparation deprives remaining bacteria of carbohydrates.

Also, demineralized dentin can be remineralized and does not need to be removed (13).

The chemo-mechanical caries removal (CMCR) techniques gained interest in dental research due to their tissue preservation potential when removing denatured dentinal collagen. This is a technique based on the dissolution of carious dentin instead of drilling, by using a chemical agent assisted by an atraumatic mechanical removal of soft carious dentin (14,15).

The 11 -point (0-10) numerical rating scale was selected for the assessment of postoperative pain and patient satisfaction, as evidence showed that this scale performs better than both a 4-point simple descriptive scale or a continuous (visual analogue) scale (16).

The results of microbiological testing in this study showed that a statistically significant reductions in the total bacterial count was found in both methods for caries removal compared to the baseline. However, no statistically significant difference was found between the two techniques.

The result revealed that no statistically significant difference was found between the papain-based gel and rotary techniques were in agreement with that found by previous studies

(3,4,7,14,17,18,19,20,21). These results are explained by the fact that brix 3000 contain “Carica

papaya” which contains many biochemically active compounds. Two especially important compounds are chymopapain and papain.

Studies conducted by Lopes et al.,2007 (1) and Al-Naimi et al.,2018 (22) and inferred that Papacarie, a papain-based CMCR material, achieving a significant reduction in total bacteria and *Streptococcus mutans* after caries removal. They attributed these results to the fact that papain acts by breaking the partially degraded collagen molecules. The action of Papain causes cleavage of the polypeptide chains and hydrolysis the crosslinks of collagen, which is an agreement with the result of the current study in the efficiency of papain-based enzyme (23,24,25).

The results of the post-operative pain and patient satisfaction showed a significant preferences towards the chemo mechanical caries removal compared to the conventional rotary method. This could be attributed to; the relatively painless technique, lack of the vibrating noisy tools and the pulpal heating and dentin desiccation potential as well as the possibility of working without local anesthetic administration. However, in this study all the preparations were done under local anesthesia to enable rubber dam application which was essential to decrease the possibility of microbial contamination during the partial caries removal.

So, the null hypothesis tested in this study, that there is no difference between Brix3000 and conventional rotary in teeth treated with partial caries removal was accepted in reduction of bacterial count. While, the hypothesis was rejected in the post-operative pain and patient satisfaction about the technique.

### Conclusion

Brix 3000 is a viable option for the minimally invasive removal of dental carious tissue, showing comparable levels of bacterial reduction, better patient satisfaction and

less post-operative pain in comparison to the conventional caries removal method.

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