OSR
ORAL SCIENCES REPORTS

Original Article

# Comparative Evaluation of Zinc Oxide Eugenol and Its Combination with Manuka Honey as Obturating Materials in Primary Molars: An *In Vitro* Study

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*Received: April 2, 2025*
*Revised: May 30, 2025*
*Accepted: July 21, 2025*

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## Abstract

**Background:** An ideal root canal filling material for primary teeth should be non-irritating, antibacterial, and non-inflammatory while ensuring ease of insertion, adhesion, and dimensional stability.

**Objectives:** This study evaluates the safety and effectiveness of manuka honey (MH) as an obturating material by comparing zinc oxide eugenol (ZOE) alone versus ZOE with MH in extracted posterior deciduous teeth.

**Methods:** This prospective *in vitro* comparative study assessed antibacterial properties using the agar well diffusion method, measuring the zone of inhibition and minimum inhibitory concentration and evaluating MH's synergistic antibacterial effect with ZOE. Handling properties, including mixing, setting, and obturation times, were recorded, and radiographic quality was evaluated based on taper, density, and length.

**Results:** Each group included 15 teeth. The mean zone of inhibition was 20.53±1.18 mm for ZOE alone (Group 1) and 22.07±1.09 mm for ZOE with MH (Group 2) ($p$=0.0021). The MIC was significantly lower in Group 2 (0.248±0.01 mg/mL) than in Group 1 (0.516±0.034 mg/mL, $p$<0.05), showing greater antibacterial efficacy. The MIC was reduced by 2.08-fold, confirming a strong synergistic effect. However, Group 1 had shorter setting (22.2±28.73 min) and obturation (4.76±0.22 min) times than Group 2 (28.73±1.28 min, 5.47±0.32 min, $p$<0.00033). Radiographic quality showed no significant difference ($p$=0.77).

**Conclusions:** Incorporating MH into ZOE improves antibacterial properties and reduces infection risk without affecting radiographic quality, making it a promising option for primary tooth obturation.

**Keywords:** antibacterial efficacy, manuka honey, obturation, pulpectomy, zinc oxide eugenol

## Introduction

Preserving primary teeth is vital in pediatric dentistry for maintaining arch integrity, mastication, and speech development. Vital pulp therapies like indirect pulp capping, direct pulp capping, or pulpotomy are suitable for reversible pulpitis. However, in irreversible pulpitis or necrosis, non-vital pulp therapy such as pulpectomy is necessary. Pulpectomy involves removing infected pulp tissue and filling the root canals with a suitable obturating material.[1] The ideal obturating material should be antibacterial, biocompatible, resorbable at the same rate as the root, radiopaque, non-irritating, and easy to insert or remove. Zinc oxide eugenol (ZOE), though commonly used for its antimicrobial and sealing properties, has drawbacks like delayed resorption and potential periapical irritation. Despite various available materials, none fulfill all ideal criteria, highlighting the challenge in managing pulpally involved primary teeth effectively until natural exfoliation.[1,2]

*Streptococcus mutans (S. mutans)* plays a key role in root canal treatment (RCT) failure due to its acid production, biofilm formation, and ability to survive in low-pH environments. It adheres strongly to dentin, resists antimicrobial agents, and persists in secondary infections, contributing to reinfection and periapical disease. Additionally, *S. mutans* degrades dentin and obturating materials, leading to microleakage and secondary caries. Its production of extracellular polysaccharides enhances biofilm protection, making eradication particularly challenging. Studies have shown that *S. mutans* can withstand intracanal medicaments like calcium hydroxide, thereby reducing treatment effectiveness. Given its frequent presence in failed RCT cases, *S. mutans* underscores the need for improved disinfection and antimicrobial strategies to ensure long-term success. Moreover, as a primary facultative anaerobe involved in early biofilm formation and dentinal caries progression, *S. mutans* can thrive under both aerobic and anaerobic conditions, making it a reliable and reproducible model organism for *in vitro* studies assessing antimicrobial efficacy and root canal disinfection.[3,4]

Natural products, such as manuka honey (MH), offer a potential alternative to conventional obturating materials.[5] While promising, their feasibility requires comprehensive biocompatibility, clinical applicability, and efficacy evaluation.[6] Recent studies have explored the effectiveness of natural compounds in paediatric endodontics, particularly their use as irrigants, intracanal medicaments, and root canal filling materials.[7] However, existing research alone may not be sufficient for clinical decision-making. Honey's antibacterial properties stem from hydrogen peroxide production via enzymatic activity, though at lower concentrations than traditional antimicrobial solutions. MH, distinguished by its Unique Manuka Factor (UMF) in New Zealand, demonstrates strong antibacterial activity and excellent biocompatibility, making it a promising candidate for endodontic applications.[8,9]

This study evaluates the safety and effectiveness of MH as an obturating material in primary teeth. While plant-derived products have long been used in therapy, and honey is recognized for its antibacterial and biocompatibility properties, its application in paediatric endodontics remains limited. The study examines Manuka honey’s antibacterial effects against *S. mutans* and its potential synergy with ZOE. Additionally, it compares the radiographic quality of obturation, including length, taper, and density, between ZOE alone and ZOE with MH to assess its suitability for root canal treatment in primary teeth.

## Materials and Methods

### *Study settings and sample collection*

This *in vitro* study involved thirty freshly extracted primary molars from children aged 4-8 years, collected at a postgraduate dental college in Eastern India, following ethical committee approval. Teeth were extracted for reasons unrelated to the study (e.g., caries or mobility) and stored in saline until use. Inclusion criteria required restorable crowns and at least two-thirds of intact root structure, with exclusions for teeth showing fractures, advanced root resorption, pathological lesions, or previous endodontic treatment. The teeth were randomly assigned into two groups (n=15 each) using a simple randomization method. Although a CONSORT diagram was not applicable due to the *in vitro* design, all procedures related to sample selection, allocation, and handling were documented to ensure transparency and reproducibility.

The sample size was determined using G*Power software, with parameters set at an effect size of 1.35, an alpha level of 0.05, and a statistical power of 80%, based on preliminary data. The calculation indicated a minimum of 11 teeth per group. To enhance reliability and account for potential variability, 15 teeth were included in each group, yielding a total sample size of 30, which was sufficient for statistical analysis.

Baseline characteristics confirmed that both groups (ZOE and ZOE+MH) were comparable. The mean age of patients was 4.5±1.5 years, with an equal gender distribution (6 males and 9 females in each group). Each group had a similar mix of first and second molars, with most teeth from the maxillary arch. All teeth exhibited adequate root integrity, and caries were the primary reason for extraction. A few teeth had existing restorations. Overall, the groups were well-matched, supporting the validity of comparative analysis (Table 1).

*Preparation combination of zinc oxide eugenol & manuka honey*

ZOE+MH was prepared by first mixing zinc oxide powder and eugenol in a 1:1 ratio to form a base paste. Then, an equal amount of MH was added relative to the volume of eugenol used (1:1 with eugenol). The mixture was blended thoroughly to achieve a thick, pliable consistency suitable for root canal obturation. The paste was applied incrementally using a folding technique, ensuring homogeneity and optimal canal filling. Fresh preparation was ensured each time to maintain the antimicrobial activity of MH.

*In vitro antibacterial assessment & evaluation of synergistic effect*

For the antibacterial assessment, the antimicrobial efficacy of MH combined with ZOE was evaluated using the agar well diffusion and microbroth dilution methods. The agar well diffusion method measured the zone of inhibition against *S. mutans* strains cultured on MH agar. At the same time, the minimum inhibitory concentration (MIC) was determined using a microbroth dilution method in a 96-well microtiter plate. Each well contained 100 µL of Mueller-Hinton Agar (MHA) medium (Figure 1). The first column served as a control with Triphenyl Tetrazolium Chloride (TTC) and *S. mutans* (MTCC 890) inoculum, while the second column contained Chlorhexidine, TTC, and *S. mutans* inoculum.[10,11] Serial twofold dilutions of the MH solution were performed starting from 50% (w/v), decreasing stepwise across the wells up to the 12$^{th}$ column, resulting in a dilution range from 50% to 0.024%. The plate was incubated at 37°C for 36-48 hours and analyzed using an ELISA reader to determine MIC values. Samples were divided into two groups: ZOE alone (n=15) and ZOE+MH (n=15). Statistical analysis was conducted using t-tests for significance and Cohen's d for effect size, with $p<0.05$ considered statistically significant.[12]

*Root canal procedure*

Thirty extracted primary molars meeting the inclusion criteria underwent pulpectomy performed by a single trained postgraduate student under the supervision of an experienced faculty member, ensuring standardized technique, consistency across procedures, and minimal operator-related variability. Carious tissue was removed using a No. 6 round bur to create straight-line access, and the pulp was extirpated with H and K hand files. The canals were irrigated with 2.5% sodium hypochlorite and normal saline to remove debris. A diagnostic radiograph determined the root canal length, and instrumentation was performed up to file size 30. The canals were obturated with two different materials after final irrigation and drying with paper points. In Group I, root canals were filled with ZOE mixed in a 1:2 powder-to-liquid ratio, and added incrementally to achieve a thick consistency. In Group II, ZOE was combined with eugenol and MH in a 1:1 ratio and applied using a folding technique. This study aimed to compare the effectiveness of these

**Table 1:** Baseline characteristics of extracted primary molars used in the study.

| Characteristic | Group 1 (ZOE) (n=15) | Group 2 (ZOE + Manuka Honey) (n=15) | Total (N=30) |
|---|---|---|---|
| Age of patients (mean ± SD) | 4.5±1.5 | 4.5±1.5 | 4.5±1.5 |
| Gender (Male/Female) | 6/9 | 6/9 | 12/18 |
| Tooth type (First/Second molar) | 8/7 | 7/8 | 15/15 |
| Arch location (Maxillary/Mandibular) | 9/6 | 10/5 | 19/11 |
| Root integrity (≥2/3 intact) | 15 | 15 | 30 |
| Presence of caries | 13 | 14 | 27 |
| Existing restorations | 2 | 1 | 3 |
| Reason for extraction | Caries/Mobility | Caries/Mobility | Caries/Mobility |

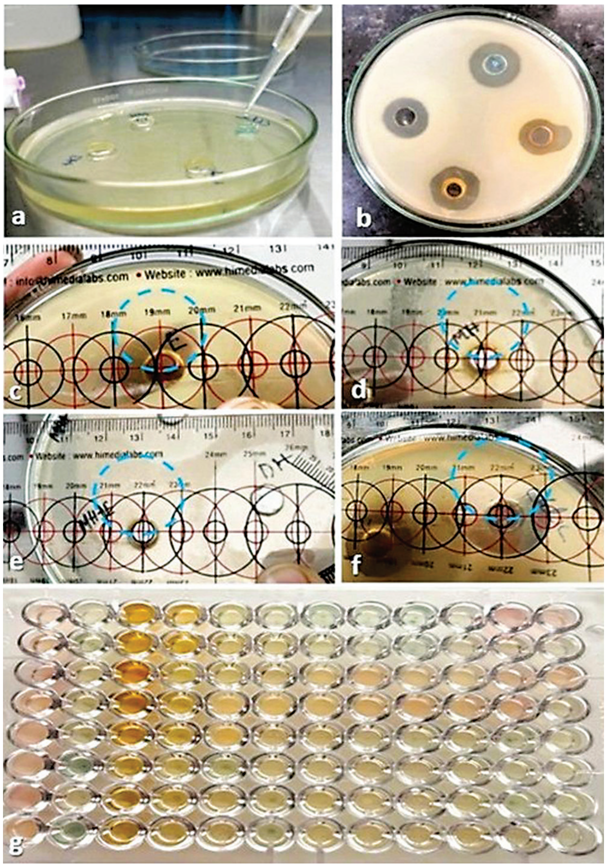


**Figure 1:** Evaluation of antibacterial properties against *Streptococcus mutans.* (a) application of extracts into wells; (b) zones of inhibition; (c) Eugenol ZOI-19mm; (d) Manuka honey ZOI-21 mm; (e) Manuka Honey with Eugenol ZOI-22mm; (f) Control group (Chlorhexidine) ZOI-22mm; (g) Minimum inhibitory concentration.

materials in primary molars, assessing whether the antimicrobial and therapeutic properties of MH could enhance the sealing ability and clinical performance of ZOE as an obturating agent.

### *Radiograph analysis*

Post-obturation periapical radiographs were taken using the paralleling technique with RVG to evaluate the quality of obturation. The radiographic quality was assessed based on three parameters: length of obturation, density of obturation, and taper of obturation. The length was categorized as adequate (within 0-2 mm of the radiographic apex), underfilled (more than 2 mm from the radiographic apex), or overfilled (beyond the apex). The density of obturation was deemed adequate if no voids were present and inadequate if voids were detected. The taper was considered adequate if it was consistent from orifice to apex and inadequate if inconsistent. To ensure unbiased evaluation, a single evaluator who was blinded to the group allocation analyzed all radiographs. Before the assessment, the evaluator underwent a calibration exercise using ten sample radiographs assessed twice at a two-week interval. Intra-examiner reliability was determined using Cohen's kappa coefficient, yielding a value of 0.87, indicating strong agreement and consistency in interpretation (Figure 2). To quantify obturation quality, a T-score system was used: a score of 4 indicated all three parameters were ideal; a score of 3 indicated two were ideal; a score of 2 indicated one was ideal; and a score of 1 indicated none were ideal (Figure 3).

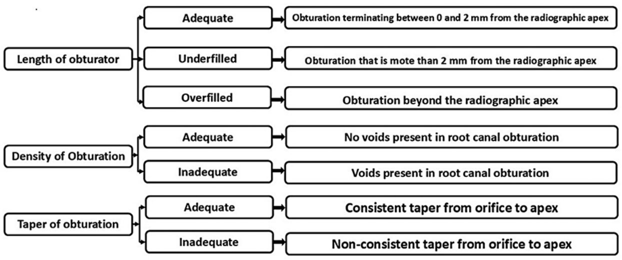


**Figure 2:** Parameters to assess root-filling radiographic quality.

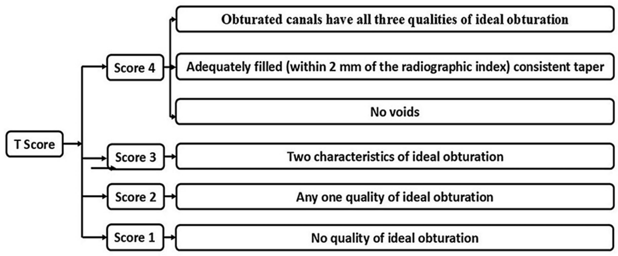


**Figure 3:** T- Score.

### *Statistical analysis*

Statistical analysis was performed using SPSS version 29. Quantitative data, such as age, were expressed as mean±standard deviation, while qualitative variables, including gender, T-score, and obturation quality, were reported as frequencies and percentages. Statistical analysis included t-tests for significance and Cohen's d for effect size, with $p<0.05$ considered significant. The Chi-square test assessed density and taper quality, while Fisher's Exact test compared obturation length and final T-score. The Shapiro-Wilk test evaluated normality, and an unpaired t-test was used to analyze manipulation time, setting time, obturation time, zone of inhibition, and MIC. A $p<0.05$ was considered statistically significant, and 95% confidence intervals were calculated for all variables.

## Results

The combination of ZOE with MH significantly enhanced its antibacterial properties against *S. mutans*. The zone of inhibition increased by 7.48% compared to ZOE alone (from 20.53 mm to 22.07 mm), indicating greater antibacterial efficacy ($p$=0.0021, Cohen's d=1.35, large effect). Additionally, the MIC was reduced by 51.94%, demonstrating a substantial improvement in antimicrobial potency ($p$<0.0001, Cohen's d=10.69, very strong effect). The MIC value showed a 2.08× reduction, further supporting the synergistic effect of MH. These findings suggest that incorporating MH into ZOE enhances its antibacterial potential, making it a promising candidate for improved dental applications (Table 2 and Figure 4).

Among 30 extracted teeth, the age ranged from 4 to 9 years, with a mean of 4.5±1.5 years. Males were 12/30 (40%), and females were 18/30 (60%). Fifteen teeth (50%) were treated with ZOE alone (Group 1), while the other 15 (50%) were treated with ZOE combined with MH (Group 2). Mixing, setting, and obturation times were measured for all the teeth. The Shapiro-Wilk test indicated a normal distribution of the data (W (15) = 0.97, $p$=0.867). Group 1 had a mean mixing time of 1.11±0.14, slightly less than Group 2 (1.17±0.14), but the difference was insignificant. The setting time was significantly shorter in Group 1 (22.2±28.73) compared to Group 2 (28.73±1.28, $p$<0.0001). The obturation time was also significantly different ($p$<0.00033), with Group 1 at 4.76±0.22 and Group 2 at 5.47±0.32 (Table 3 and Figure 5).

Periapical radiographs were evaluated after obturation to assess the quality of root canal fillings based on length, density, and taper (Figure 6 and Figure 7). T-scores were calculated accordingly. In Group I (ZOE), 7 out of 15 teeth (46.6%) had adequate obturation length, 5 (33.3%) were underfilled, and 3 (20%) were overfilled. Adequate density was observed in 11 teeth (73.3%), while 4 (26.6%) showed inadequate density. Ten teeth (66.6%) had an adequate taper, and 5 (33.3%) were inad-

**Table 2:** Antibacterial properties and synergistic effect of zinc oxide eugenol + manuka honey against *Streptococcus mutans.*

| Parameter | ZOE (n=15) | ZOE + MH (n=15) | *p*-value | 95% Confidence Interval | Synergistic Effect (ZOE + MH) |
|---|---|---|---|---|---|
| Zone of Inhibition (mm) | 20.53±1.18 | 22.07±1.09 | 0.0021 | 7.6683 to 31.0317 | ↑ 7.48% (Cohen's d = 1.35, large effect) |
| SEM (Zone of Inhibition) | 0.31 | 0.28 | — | — | — |
| Minimum Inhibitory Concentration (MIC) (mg/mL) | 0.516±0.034 | 0.248±0.01 | < 0.0001 | 0.35073 to 0.61327 | ↓ 51.94% (Cohen's d = 10.69, very strong effect) |
| SEM (MIC) | 0.0089 | 0.0026 | — | — | — |
| MIC Fold Reduction | — | — | — | — | 2.08× reduction in MIC |

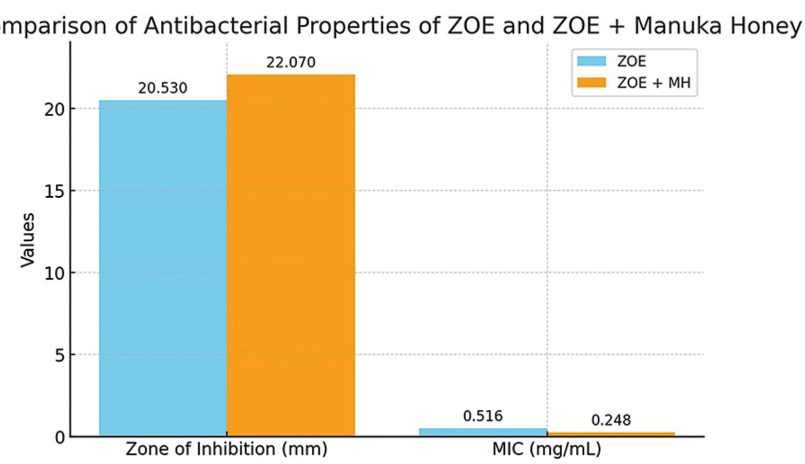


**Figure 4:** Bar graph comparing the Zone of Inhibition (mm) and Minimum Inhibitory Concentration (MIC, mg/mL) for zinc oxide eugenol and zinc oxide engenol+manaka honey against *Streptococcus mutans.*

**Table 3:** Mean of manipulation and obturation time for both groups.

| Parameters | | ZOE (n=15) | ZOE+MH (n=15) | *p*-value | 95% Confidence interval |
|---|---|---|---|---|---|
| Mixing time | Mean±SD | 1.11±0.14 | 1.17±0.14 | 0.2504 | -0.0486 to 0.1632 |
| | SEM | 0.0363 | 0.0368 | | |
| Setting time | Mean±SD | 22.2±28.73 | 28.73±1.28 | < 0.0001 | -7.98 to -5.08 |
| | SEM | 0.63 | 0.33 | | |
| Obturation time | Mean±SD | 4.76±0.22 | 5.47±0.32 | 0.0033 | 0.5037 to 0.9203 |
| | SEM | 0.0570 | 0.0842 | | |

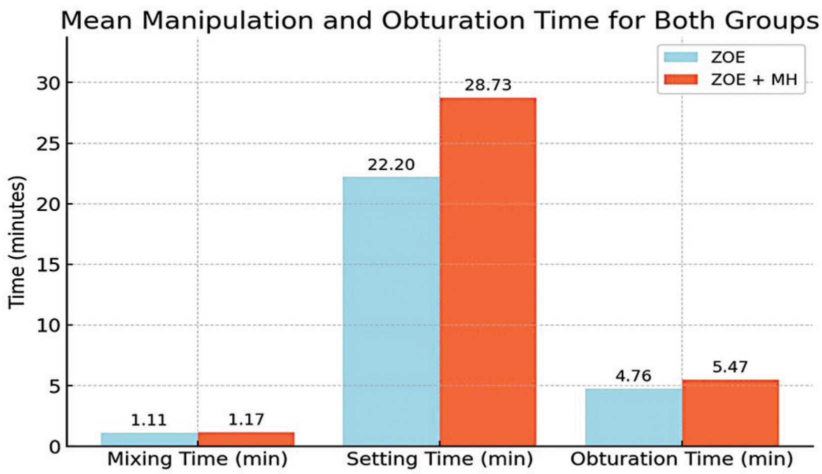


**Figure 5:** Bar graph comparing the mixing time, setting time, and obturation time for zinc oxide eugenol and zinc oxide eugenol+manuka honey.

**Table 4:** Radiographic analysis for quality of obturation.

| Parameter | Quality | ZOE [n (%)] | ZOE+MH [n (%)] | *p*-value |
|---|---|---|---|---|
| Density of obturation | Grade 1 (Adequate) | 11 (73.3%) | 9 (60%) | 0.4386 |
| | Grade - 2 (Inadequate) | 4 (26.6%) | 6 (40%) | |
| Length of obturation | Grade 1 (Adequate) | 7 (46.6%) | 5 (33.33%) | 0.889 |
| | Grade - 2 (Underfilled) | 5 (33.3%) | 7 (46.67%) | |
| | Grade 3 (Overfilled) | 3 (20%) | 3 (20%) | |
| Taper of obturation | Grade 1 (Adequate) | 10 (66.66%) | 12 (80%) | 0.4090 |
| | Grade - 2 (Inadequate) | 5 (33.33%) | 3 (20%) | |
| T score | Score 1 | 0 | 0 | 0.770008 |
| | Score 2 | 5 (33.33%) | 6 (40%) | |
| | Score 3 | 7 (46.6%) | 8 (53.33%) | |
| | Score 4 | 3 (20%) | 1 (6.67%) | |

equate. In Group II (ZOE + MH), 5 teeth (33.3%) showed adequate length, 7 (46.6%) were underfilled, and 3 (20%) were overfilled. Density was adequate in 9 teeth (60%) and inadequate in 6 (40%). Twelve teeth (80%) had an adequate taper, and 3 (20%) were inadequate. T-scores were assigned based on how many parameters met the ideal criteria. In Group I, 5 teeth (33.3%) scored 4, 7 (46.6%) scored 3, and 3 (20%) scored 2. In Group II, 1 tooth (6.67%) scored 4, 8 (53.3%) scored 3, and 6 (40%) scored 2. No tooth in either group scored 1. Statistical analysis showed no significant difference between the two groups in obturation quality ($p>0.05$) (Table 4 and Figure 8).

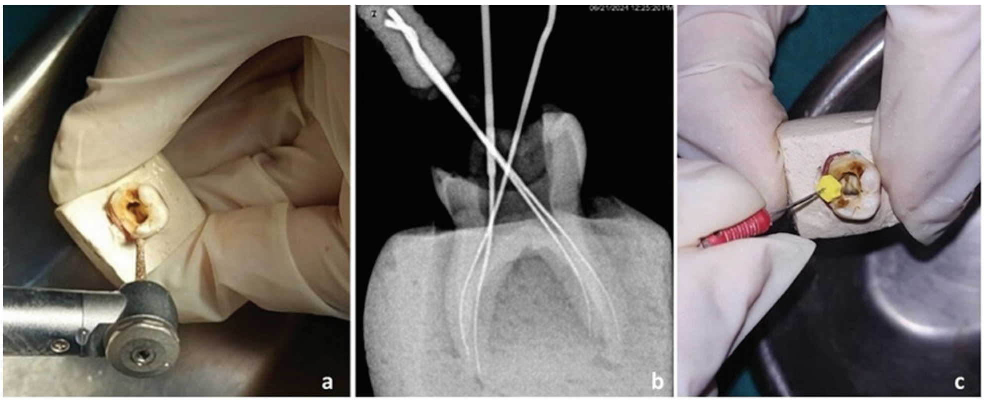


**Figure 6:** Root canal preparation (a) access opening using high-speed airotor; (b) working length determination using radiographic technique; (c) shaping and cleaning of canals using k-files.


**Figure 7:** Postoperative Radiographs. (a) Radiograph of Group A; (b) Radiograph of Group B.

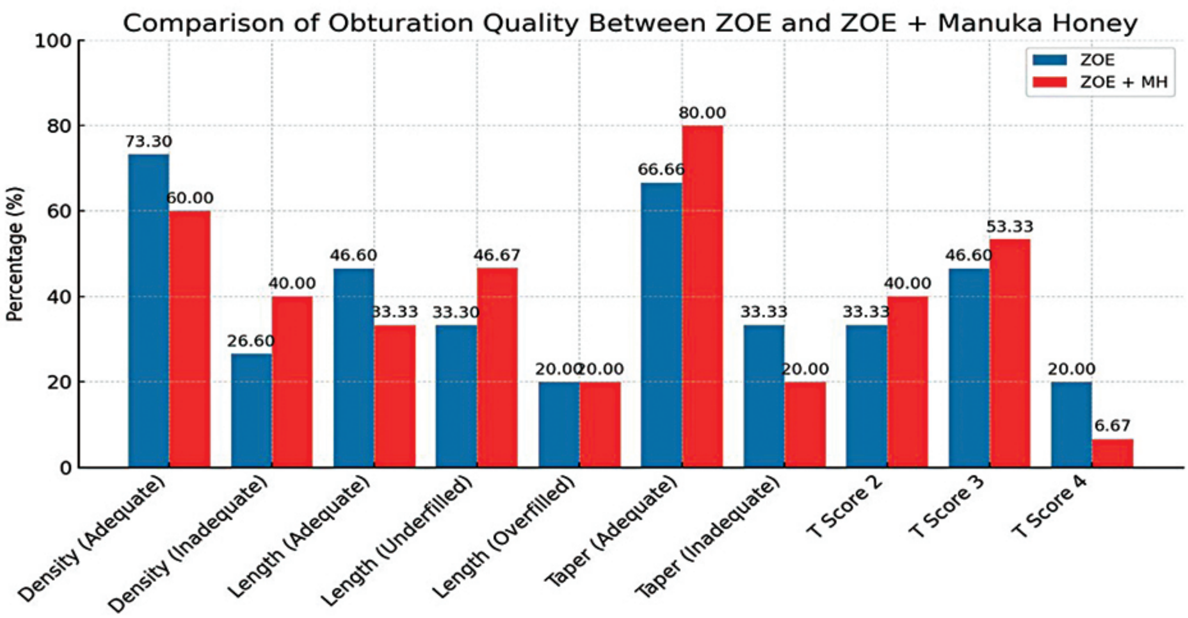


**Figure 8:** Bar graph comparing the obturation quality parameters (Density, Length, Taper, and T Score) between zinc oxide eugenol and zinc oxide eugenol+manuka honey.

## Discussion

This *in vitro* study demonstrated that the incorporation of MH into ZOE) significantly enhanced its antibacterial efficacy. The combination exhibited a larger mean zone of inhibition (22.07±1.09 mm) compared to ZOE alone (20.53±1.18 mm; $p$=0.0021), and a lower MIC value (0.248±0.01 vs. 0.516±0.034; $p$<0.0001). These results indicate a statistically significant improvement in antimicrobial activity. However, it is important to acknowledge that *in vitro* antibacterial findings may not directly correlate with clinical effectiveness. Improved inhibition zones or MICs do not necessarily translate to better healing, reduced postoperative infection, or long-term success *in vivo*. Therefore, while promising, these results should be interpreted with caution until further clinical evidence is available.

Manuka honey's antimicrobial effects are attributed to several unique components, including methylglyoxal (MGO), D-glucono-δ-lactone, and hydrogen peroxide, which inhibit bacterial replication, disrupt biofilm formation, and contribute to acidification of the local environment.(13-15) Its low water activity (0.6-0.75) further limits microbial growth.(13,15) Although there is evidence supporting the antibacterial efficacy of MH, studies comparing the duration or sustained effects of MH relative to ZOE remain limited. While MH is known to reduce biofilm formation and promote healing, claims regarding its prolonged antibacterial action over ZOE alone require further validation.(15-19)

Radiographic analysis showed that both ZOE and ZOE-MH groups achieved comparable obturation quality. No significant differences were observed in obturation length, density, or taper between the groups. T-score analysis further supported these findings, with slight, non-significant differences. Although the addition of MH led to marginally increased mixing, setting, and obturation times, these remained within acceptable clinical thresholds, suggesting that usability was not compromised.(16,20)

ZOE remains one of the most commonly used root canal filling materials in primary teeth due to its biocompatibility and antibacterial properties, especially against *E. faecalis, S. mutans*, *E. coli,* and *S. aureus.*(21,22) However, limitations such as delayed resorption, potential irritation of periapical tissues, and interference with permanent tooth eruption have been reported.(14,23) Eugenol, a key component of ZOE, exhibits anti-inflammatory and analgesic effects, though its levels decline significantly within weeks of placement.(24,25) The addition of MH to ZOE may help mitigate these shortcomings by offering complementary antimicrobial and anti-inflammatory benefits.(13-17)

## Limitations and future research

Nonetheless, several limitations must be addressed. The sample size in this study was small (n=30), limiting statistical power and generalizability. The radiographic assessment involved a degree of subjectivity, and inter-examiner reliability was not evaluated. Moreover, the use of a single bacterial species *(S. mutans)* does not reflect the polymicrobial nature of pulpal infections. Being an *in vitro* study, it cannot replicate the complexity of clinical conditions, including host immune responses and oral environmental variables.(19) Future studies should include randomized controlled trials with larger cohorts, long-term follow-ups, and assessments against diverse microbial flora. Comparative evaluations with other pediatric obturating materials such as Metapex, Endoflas, and calcium hydroxide would also help determine the broader applicability of ZOE-MH in pediatric endodontics. While MH enhances the antimicrobial potential of ZOE, further clinical validation is essential before it can be recommended as a standard adjunct.

## Conclusions

ZOE demonstrated strong antibacterial properties, and the addition of MH further enhanced its antimicrobial efficacy. However, both materials showed comparable results in terms of obturation quality. These findings indicate the potential advantage of incorporating MH into pulpectomy procedures to enhance antibacterial action. Nevertheless, further *in vivo* studies with larger sample sizes are required to validate its clinical applicability.

## Funding

No funding received.

## Conflicts of Interests

The authors declare no conflicts of interest.

## Ethical Permission

The study was conducted after the approval of the Institutional Ethical Committee vide letter no. IEC-IDS/IDS/SOA/2023/I-31 date 21 December 2023.

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