





## Article

# A Comparative Study to Evaluate the Effect of Honey and Zinc Oxide Eugenol Dressing for the Treatment of Dry Socket: A Double-Blind Randomized Controlled Trial

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**Abstract:** Dry socket is a common postoperative complication secondary to any tooth extraction but is more commonly associated with mandibular third molars. Dry socket has been treated with various treatment modalities with different success rates. This study aimed to evaluate the effect of using honey and zinc oxide eugenol as an intra-socket medicament for the treatment of dry sockets. Ninety patients were divided into three groups as follows: Group 1 “honey”: 30 patients; Group 2 “zinc oxide eugenol”: 30 patients; and Group 3 “control”: 30 patients. Pre-medication and post-medication pain scores at different time intervals were measured on a verbal rating scale. The mean ages of the patients in each of the groups were as follows: Group 1:  $44.26 \pm 14.14$ ; Group 2:  $45.30 \pm 18.08$ ; and Group 3:  $51.93 \pm 9.75$ . As regards verbal rating scale pain scores, a significant difference was noted in patients that belonged to Groups 1 and 2, with an immediate reduction in post-medication pain scores. However, patients belonging to Group 3 reported pain and discomfort for over a week. The use of honey and zinc oxide eugenol resulted in significant immediate post-medication pain scores in patients as compared to the control group. Therefore, both honey and zinc oxide eugenol can be used as treatment options for dry socket patients.

**Keywords:** dry socket; honey; dental extractions; propolis; zinc oxide eugenol

## 1. Introduction

After performing dental extractions, dry socket is one of the most frequently encountered postoperative complications [1]. Dry socket is also referred to as necrotic socket, fibrinolytic socket, alveolar osteitis (AO), alveolitis, sicca dolorosa, and localized osteitis [2]. Although dry socket can be encountered in any tooth, it is associated more frequently after mandibular third molar extraction, being the extraction that is essential to the beginning of dry socket [3]. Dry socket develops as a postoperative complication when a blood clot fails to develop, dissolves, or dislodges at the site of the extraction before the socket is healed [4]. Clinically, a dry socket is visible as part or all of the bone around the occlusal perimeter or within the socket exposed a few days after the extraction. The incidence of

post-extraction complications overall is 8.4% for the mandibular teeth; among them, 4.2% are reported to be dry socket, while in the maxilla, 5.9% of complications are reported overall, 0.4% of which being dry socket [5,6]. The incidence of dry socket varies between 1% and 5% of all dental extractions, with up to 38% of dry socket cases associated with mandibular third molars [7,8]. Studies report that insufficient blood supply is one of the primary reasons for site-specificity of development of dry socket; however, increased bone density, excessive forces during extraction, and decreased capacity of producing granulation tissue are responsible factors too [9–11]. Moreover, risk factors for increasing the probability of developing dry socket include use of oral contraceptives, bacterial causes, infection, previous history of experiencing dry socket, and smoking [12]. Factors such as age, sex, medical history, extraction site, amount of anesthesia, and operator experience have no effect on the observation of dry socket [13].

The socket that has been left exposed might be accumulated with food debris and bacterial biofilms that further hinder the healing process of the socket. Moreover, bacteria collected inside the socket may even ferment the food particles inside it, which in turn exacerbates the already compromised situation of the socket. Most commonly, patients suspected of suffering from dry socket present with acute pain from the exposed socket that lingers for many days until the socket is completely covered by the epithelium.

Before management, clinicians focus on preventing the development of dry sockets with the use of chlorhexidine mouthwash preoperatively, use of antibiotics such as penicillins, clindamycin, metronidazole, and erythromycin, antifibrinolytics such as tranexamic acid, and antimicrobial photodynamic therapy (ADPT) [14]. Management of dry sockets has varied among clinicians, depending on their expertise and experience with dealing with dry sockets. Traditionally, the treatment of dry socket has been irrigation, surgical intervention, and placement of medicated dressings. Irrigation is performed which removes the debris, sequestra, and bacteria from the exposed bone surface of the dry socket. Most commonly, the irrigation solutions used in the dry socket are chlorhexidine gluconate and normal saline [15]. Medicated dressings are then placed in the socket, which promotes healing and reduces patient symptoms. Commonly applied dressings include Alvogyl and zinc oxide eugenol (ZOE) after irrigation of the socket. One study reports Alvogyl to be more effective than ZOE by providing a short time of complete pain relief, fewer visits needed to change the dressings, and, lastly, faster healing of the socket [16]. Natural medicines have been used for many decades, as they tend to have few to no side effects as compared to pharmaceutically produced drugs. Honey is one such product that has previously been used to treat many infections, as its use has been found to make the infectious wound sterile in 3–6 days [17]. One of the active ingredients of honey is propolis. Propolis has been used in the field of dentistry and medicine primarily due to its antibacterial, anti-inflammatory, analgesic, and antifungal properties [18]. One study in the literature reports the use of propolis in dental sockets which resulted in accelerated epithelial repair after tooth extraction [19]. A study by Ansari et al. found that the use of honey in the treatment of dry socket produced no side effects along with a significant reduction in inflammation, and hyperemia, which led to a reduction in the pain and discomfort experienced by the patient [17]. Moreover, one study reports that the use of honey in patients suffering from dry socket results in healing of the socket in one week, with a significant reduction in C-reactive protein (CRP) levels as compared to pre-treatment levels, which indicates faster recovery [20].

Thus, this study aimed to compare the effectiveness of honey and zinc oxide eugenol dressings placed as intra-alveolar socket dressings for the management of dry socket and to identify the most effective and best among them. The findings of this study will provide evidence as to whether the use of honey and zinc oxide eugenol can be considered as effective treatment options for patients suffering from dry socket.

## 2. Materials and Methods

This double-blind randomized controlled trial was carried out from 7 March to 12 August 2021 in the Department of Oral and Maxillofacial Surgery at the College of Dentistry, Jouf University, Saudi Arabia. This was an interventional study, carried out using quasi-experimental design. To calculate the sample size, OpenEpi software was used. A mean value of  $2.567 \pm 2.67$  for pain severity was considered. The power of the test was 80% and the confidence interval (CI) 95%; the sample size for each of the three groups was 30 participants. Thus, a total of 90 patients were included in the present study.

The Ethical and Review Board of Jouf University approved this study (Ethical review number: 11-04-42), and all of the procedures in this study were in compliance with the Helsinki Declaration and its amendments. This trial has been registered under the Saudi Clinical Trial Registry (SCTR) with application no. 21021702. Informed and written consent was taken from the participants before they were included in this trial study. The inclusion criteria were patients above the age of 18 of both genders who underwent extraction of teeth and were clinically diagnosed with dry socket at the clinic of the College of Dentistry, Jouf University, Saudi Arabia. Patients who were below the age of 18 years or above 70 years of age; had various bone diseases, including osteoporosis; had a history of taking oral or intravenous bisphosphonates; and had a history of radiotherapy on the head, neck, and jawbones were excluded from this study.

After demographic characteristics of patients were determined and clinically diagnosed with dry socket, they were assigned numbers from the first to the 180th patient and randomly allocated via lottery method to three groups numbered 1, 2, and 3. Group 1: patients were treated with honey (Al Shifa, 100% pure, certified by Saudi Arabian Standards Organization (SASO)) soaked into sterile gauze as a dressing; Group 2: patients were treated with zinc oxide eugenol (SPIDENT EsTemp zinc oxide eugenol temporary cement) gauze dressing (a gauze piece soaked with freshly prepared ZOE paste), which was placed into the socket; Group 3: patients were treated with normal saline rinse as control. The types of treatment and medication provided to the patients were beneficial and non-harmful according to medical ethics, with approval from the institutional ethics committee. Confounding variables such as age, gender, and history of pain were controlled by matching. The medications were placed in unmarked identical bottles and the saline was placed in a covered syringe, all without the original labels on them, and marked as Group 1, 2, and 3.

Patients were allowed to continue their oral analgesic medication, namely ibuprofen 200 mg, 400 mg, or 600 mg twice daily, depending upon the severity of initial pain upon diagnosis. Pain relief was recorded and compared between the three groups on a visual analog pain scale at every appointment. The intra-alveolar packing was changed until the postoperative pain symptoms subsided. Patients were reviewed at 5 min post-medication, 30 min post-medication, 60 min post-medication, 2nd day post-medication, 4th day post-medication, and 7th day post-medication. The patients were requested to note daily pain records on a (0–10) visual analog scale, with 0 representing no pain and 10 representing the worst pain.

For safety purposes, any harmful effects of the medications were also recorded. Patients were instructed to call the investigator immediately about any problem; in such circumstances, treatment was immediately terminated and discontinued. The patient was requested to visit the investigator at the earliest possible time. If no side effects were noted, the treatment option was repeated a maximum of four times over a period of two weeks to assess the complete effect of the medication in case complete relief was not achieved the first time. The total time required for complete healing and the number of repeated sessions for each medication until complete relief from all symptoms were recorded in Performa, attached as Annexure (see Supplementary Materials).

The success rate of the procedure was categorized into: excellent, good, fair, and poor, according to pain relief, the need to use oral analgesics, and the number of repeated sessions for each medication.

Excellent: complete relief of pain without use of analgesics; pain score = 0 (no pain)

Good: complete relief of pain with modest use of analgesics (200 mg ibuprofen); pain score: 1–3 (mild)

Fair: complete relief of pain with moderate use of analgesics (400 mg ibuprofen); pain score: 4–6 (moderate pain)

Poor: continued pain despite high dose of analgesics (600 mg ibuprofen); pain score 7–10 (severe pain)

The procedure was double-blind, as both the patient and investigator did not know about the medication dressing applied and the follow-up was performed by an independent investigator blinded from the original identity of all groups for documentation of the final outcome.

#### Data analysis:

The data were analyzed in SPSS-25. Descriptive analysis was carried out to calculate mean and standard deviation, percentage, and frequency of quantitative and qualitative variables, i.e., age, gender, scores of VAS scale, values for different study groups assigned, and severity of pain categories. An independent *t*-test was used to check gender disparities. A paired *t*-test was used to compare the outcome of the different groups assigned. A chi-square test was used to control confounders. A *p*-value of  $\leq 0.05$  was considered statistically significant.

### 3. Results

This was a double-blind randomized controlled trial that consisted of 90 patients randomized into three groups as follows: Group 1: honey; Group 2: zinc oxide eugenol; and Group 3: control. One patient was lost to follow-up from the control group due to unknown reasons, and so they were not included in the statistical analysis. As presented in the CONSORT flow diagram (Figure 1). The mean ages of the participants in each group are as follows: Group 1 (honey):  $44.26 \pm 14.14$ ; Group 2 (zinc oxide eugenol):  $45.30 \pm 18.08$ ; and Group 3 (control):  $51.93 \pm 9.75$ . Regarding gender, the distribution of males and females in each group is as follows: Group 1: 20 and 10; Group 2: 13 and 17; and Group 3: 13 and 17. Moreover, in this study, 20 (33.6%) cases of alveolar osteitis appeared after anterior teeth extractions, while 70 (66.3%) cases presented in patients after posterior teeth extractions in both upper and lower dental arches. The incidence of dry socket was 42 (46.66%) cases in maxilla and 48 (53.33%) cases in mandible, as presented in Table 1.

**Table 1.** Incidence of dry socket in participants ( $n = 90$ ).

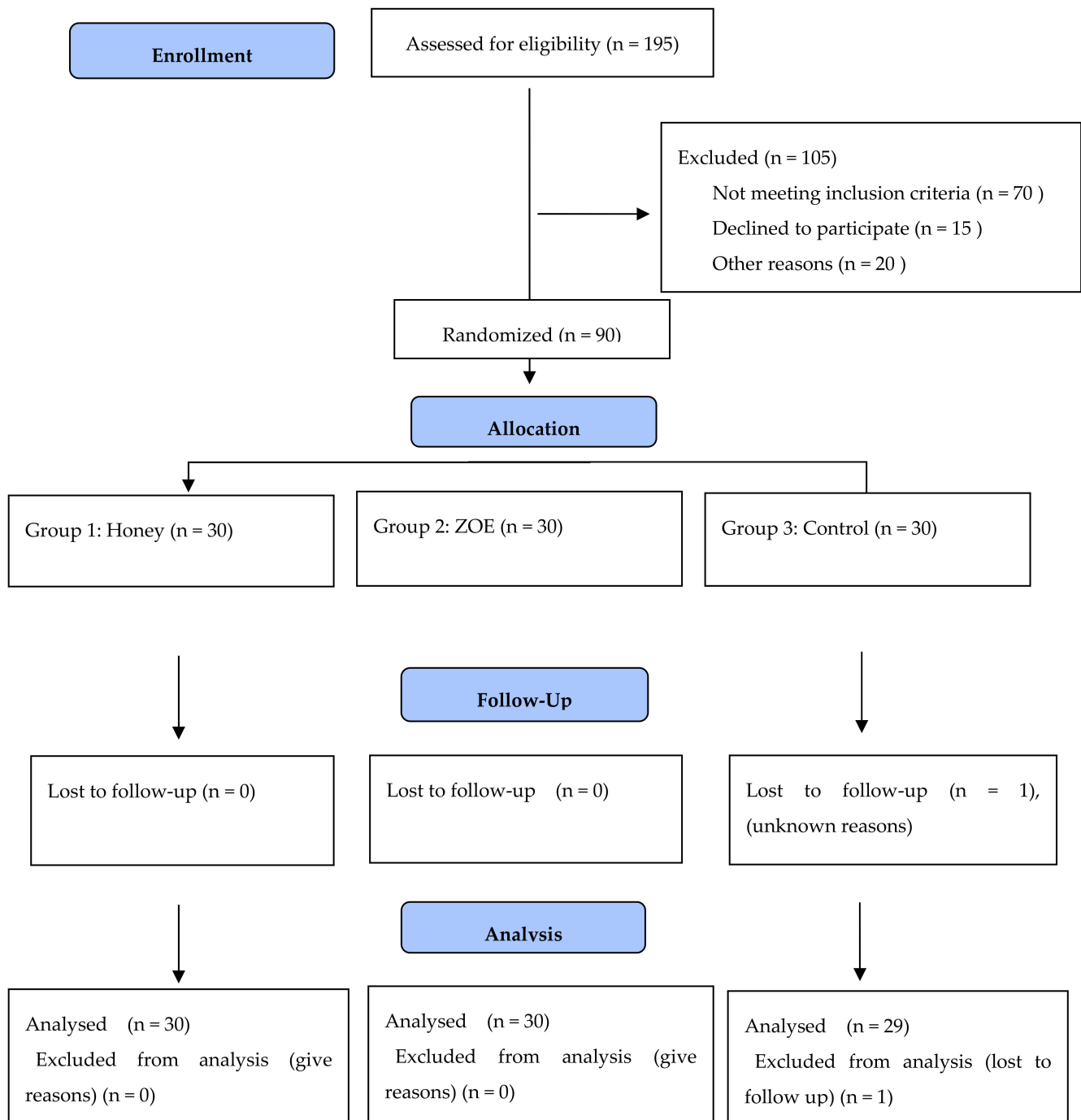
Region in the Arch	Teeth	Maxilla		Mandible	
		Single Extraction	Multiple Extraction	Single Extraction	Multiple Extraction
Anterior	Incisor	NR	8 (40%)	NR	10 (50%)
	Canine	2 (10%)	NR	NR	NR
Posterior	Premolar	NR	7 (10%)	NR	12 (17.14%)
	Molar	11 (15.71%)	14 (20%)	10 (14.28%)	16 (22.85%)

NR: not reported.

The incidences of pre-medication pain VAS scores of the participants are presented in Table 2.

**Table 2.** Premedication VAS score of participants of all groups.

Groups	N	Mean	Standard Deviation
Group 1: Honey	30	8.50	0.97
Group 2: Zinc Oxide Eugenol	30	8.90	0.76
Group 3: Control (Normal Saline)	29	8.10	0.80



**Figure 1.** CONSORT flow diagram of the study.

Mean VAS scores at 5 min post-medication, 30 min post-medication, 60 min post-medication, 2nd day post-medication, 4th day post-medication, and 7th day post-medication of all groups are presented in Table 3. Regarding post-medication VAS pain scores of participants of all three groups, the majority of the patients reported a significant reduction in pain scores from 5 min post-medication as compared to the control group. After 60 min post-medication, the majority of the patients reported minimal pain, with patients belonging to the control group experiencing higher pain levels as compared to Groups 1 and 2. Most of the patients on the second day were pain-free in both Groups 1 and 2. However, patients belonging to Group 3 became pain-free on the 7th postoperative day, as presented in Table 4. Most of the patients suffered from moderate pain in all of the three groups after 5 min post-medication. The level of pain score declined to mild in both Groups 1 and 2

after 30 min; however, patients in Group 3 still suffered from moderate pain. On the second day, the pain score of all patients in the three groups was mild, and so patients took 200 mg ibuprofen. From the fourth day onwards, all of the patients in the three groups were pain free.

**Table 3.** Mean VAS scores of all groups.

Groups	5 min Post-op VAS Score Mean $\pm$ SD	30 min Post-op VAS Score Mean $\pm$ SD	60 min Post-op VAS Score Mean $\pm$ SD	2nd day Post-op VAS Score Mean $\pm$ SD	4th day Post-op VAS Score Mean $\pm$ SD	7th day Post-op VAS Score Mean $\pm$ SD
Group 1: Honey	4.26 $\pm$ 0.73	2.20 $\pm$ 0.71	1.16 $\pm$ 0.69	0.33 $\pm$ 0.48	0.06 $\pm$ 0.25	0.00 $\pm$ 0.00
Group 2: Zinc Oxide Eugenol	4.40 $\pm$ 0.81	1.93 $\pm$ 0.25	0.93 $\pm$ 0.25	0.00 $\pm$ 00	0.00 $\pm$ 00	0.00 $\pm$ 00
Group 3: Control	5.83 $\pm$ 0.38	4.60 $\pm$ 0.50	2.00 $\pm$ 0.00	1.00 $\pm$ 0.00	0.60 $\pm$ 0.50	0.00 $\pm$ 00

**Table 4.** Comparison of VAS scores among the three groups using paired *t*-test.

Groups	Mean	Standard Deviation	Standard Error Mean	<i>t</i> -Value	df	<i>p</i> -Value
Group 1: Honey and Group 2: Zinc Oxide Eugenol	0.13	0.57	0.10	1.23	29	0.229
Group 1: Honey and Group 3: Control	−1.00	0.43	0.08	−12.58	29	0.001
Group 2: Zinc Oxide Eugenol and Group 3: Control	−1.12	0.22	0.04	−28.41	29	0.001

Regarding gender, an independent *t*-test was used to evaluate the difference between VAS pain scores. No significant difference was found in VAS scores of males and females, as presented in Table 5.

**Table 5.** Gender disparities between all groups using independent *t*-test.

Gender	N	Mean	Standard Deviation	Standard Error Mean	Mean Difference	<i>t</i> -Value	df	<i>p</i> -Value
Male	45	1.84	0.84	0.12	−0.31	−1.82	87.87	0.07
Female	44	2.15	0.76	0.12				

#### 4. Discussion

Dry socket is a common postoperative complication that patients experience, mostly associated with mandibular third molar extraction due to an end arterial blood supply. The pain of dry socket is described by patients to be excruciating, which demands timely and proper treatment in order to relieve the pain and discomfort of the patients. Many risk factors have been associated with a tendency to develop dry socket, such as traumatic extraction, smoking, oral contraceptives, female gender, and suppression of the immune system [21].

In our study, most of the patients suffered severe pain on average, with a verbal rating score of 8. Similar findings have been reported in a study by Bortouzzi et al., where patients did suffer from severe pain due to dry socket [22]. The severe pain of dry socket originates primarily from the exposure of the underlying bone to the oral environment, which is supplemented by the action of bacteria that further exacerbates the condition.

Firstly, in our study, patients who were assigned to the honey dressing treatment modality for dry socket had a significant decrease in the pain score immediately after the



placement of honey, as compared to their pre-treatment pain scores. Such results have also been reported in a study by Ansari et al., who concluded in their study that the use of honey in patients with dry socket results in a significant increase in the healing of the dry socket along with a reduction in discomfort for the patient [17]. Furthermore, another study also concluded that the use of honey in dry socket patients resulted in a decrease in hyperemia, inflammation, exudation, edema, pain, and discomfort for the patient along with a soothing effect [23]. Honey has been known to keep the wound moist, speeds up the healing process, reduces scarring, and dehydrates the bacteria through its hygroscopic property, thereby rendering the bacteria inactive [24,25]. Moreover, honey is also responsible for angiogenesis and granulation, which further enhances the speeding up of the healing process [26]. Thus, all of these characteristics make honey a suitable choice as an effective treatment option for patients suffering from dry socket.

One of the active ingredients of honey is propolis. Propolis has a wide application in dentistry, including dental caries and oral infections. A study by Serrano et al. found that the use of propolis in dental sockets may be beneficial in preventing dry socket after extraction of impacted third molars [27]. Although propolis is known for its analgesic, antibacterial, and anti-inflammatory properties, its use in dry socket is yet to be explored; hence, further studies must be carried out to explore its effect in patients suffering from dry socket.

Secondly, in our study we used zinc oxide eugenol as a medicated dressing in patients who were assigned to Group 2. The results obtained from our study show that there was a significant reduction in immediate post-medication pain scores as compared to pre-treatment scores. Such results agree with a study by Chaurasia et al., which concluded that patients reported significant immediate post-medication pain relief after placement of zinc oxide eugenol as an intra-socket medicament [28]. However, one study found Alvogyl to be superior in relieving pain as compared to zinc oxide eugenol [29].

Along with the use of honey, zinc oxide eugenol, and Alvogyl, different methods have been studied in the literature in the management of dry socket. The use of concentrated growth factor (CGF) and low-level laser therapy (LLLT) has been studied and has reported significant pain reduction in patients suffering from dry socket as compared to conventional treatment comprising saline irrigation and socket curettage [30]. Furthermore, the use of platelet rich fibrin (PRF) has been proven to be an established treatment option for dry socket, due to its wound-healing properties and significant reduction of pain in the patients [31].

Experience and tolerance of pain differ among the genders. In our study, there was no significant difference in the pain scores of males and females. Such findings contrast with a previous study where females were found to have higher pain scores as compared to males [32]. Furthermore, female gender has not been found to be a risk factor for developing dry socket according to a study by Younis et al. [13].

Dry socket is a condition that has an array of treatment options. According to our study, zinc oxide eugenol and honey are considered effective in relieving pain and discomfort in patients. Despite the strengths of this study, such as adequate patient follow-up and keeping track of pain scores, there were some limitations. Firstly, this study included a small sample size of patients, and patients might have continued smoking despite the instructions provided to them. Lastly, in this study we did not evaluate healing in the postoperative phase.

## 5. Conclusions

The use of honey or zinc oxide eugenol as an intra-socket medicament resulted in a significant reduction in immediate pain scores in patients as compared to the use of normal saline irrigation alone. Therefore, zinc oxide and honey can be effectively used to treat dry socket as an adjunct to other standard treatment modalities.

**Supplementary Materials:** The following is available online at <https://www.mdpi.com/article/10.3390/app12010006/s1>, Annexure I Proforma for data collection for Project title: A Comparative Study to Evaluate The Effect of Olive oil, Black seed powder, Honey, Nano-biofusion Gel Alvogly And Zinc Oxide Dressing for the Treatment of Dry Socket: A Double Blind Randomised Control Study.

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**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** The data included in the present study are available upon request from the corresponding author.

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**Conflicts of Interest:** The authors declare no conflict of interest.

## Abbreviations

VAS	Visual analog scale
CRP	C-reactive protein
ZOE	Zinc oxide eugenol
ADPT	Antimicrobial photodynamic therapy
CGF	Concentrated growth factor
LLLT	Low-level laser therapy

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