Dentistry 3000
Vol 11 No 1 (2023) DOI 10.5195/d3000.2023.380

The effectiveness of Turmeric gel in the healing of donor site for Free Gingival Graft

Zuhir Alasfar[1], Rowaida Saymeh[1], Mays Khazem[2]

[1]*Faculty of Dentistry, Damascus University, Syria*

[2]*Faculty of Pharmacy, Damascus University, Syria*

Abstract

BACKGROUND: Preparation of turmeric extract gel with a concentration of 10% and comparing it with non-eugenol gingival dressing (Coe-Pak™) in the healing and re-epithelialization of palatal donor site after free gingival graft, and reduction of postoperative pain.

MATERIALS AND METHODS: This study was conducted on twenty-two patients with lack of attached gingival tissue for various reasons and received soft tissue augmentation via free gingival grafts. Participants were randomly divided into two equal groups: group I (test) was treated with 10% turmeric gel while group II (control) was treated with (Coe-Pak™). Both pain level index which assessed by using the Visual Analogue Scale (VAS) and Analgesic consumption index were recorded for 7 days after surgery. The healing index, the color match index, and the re-epithelialization index were assessed on days 7, 14, 21, and 28. Finally, wound size index was measured via periodontal Probe at baseline and days 7, 14, 21, 28, and after 2 months.

RESULTS: Group I showed significant pain reduction measured by VAS and analgesic consumption on day 3, 4, 5, 6, 7 ($p<0.05$) with no significant difference on the first two days ($p>0.05$). Group I demonstrated significant acceleration in the initial healing process during the 1st week ($p=0.002$) and 2nd week ($p=0.01$) with no significant difference between both groups in the 3rd and 4th weeks ($p>0.05$). Group I showed statistically higher VAS for the color match on day 7, 14, 21, and 28. No statistical difference was noted between the groups after two months. There was no statistical difference between groups I and II in the re-epithelialization and wound size index at any of the follow-up periods ($p>0.05$).

CONCLUSION: 10% turmeric extract gel showed relief of post-operative pain, acceleration of the healing process, and better outcomes in terms of the color match for the palatal wound after free gingival grafting procedure comparing to the Coe-Pak™ periodontal dressing.

KEYWORDS: Curcumin; Free gingival graft; periodontal dressing; donor site

Citation: Alasfar, Z et al. (2023) The effectiveness of Turmeric gel in the healing of donor site for Free Gingival Graft
Dentistry 3000. 1:a001 doi:10.5195/d3000.2023.380
Received: August 8, 2022
Accepted: March 11, 2023
Published: April 7, 2023

Email: zuhiralasfar@gmail.com

Introduction

Free gingival graft (FGG) has been used for treating gingival recession and is considered the most common technique for soft tissue augmentation around teeth and dental implants [1]. However, postoperative discomfort associated with the presence of two surgical sites, one of which is usually the palate, limits the usage of this technique and requires alternative treatments with less associated morbidity [2]. Bjorn, one of the pioneers in the field, described FGG in 1963 [3] as a technique that impedes the recession progress, facilitates plaque control, and reduces or eliminates root sensitivity [4, 5]. Miller has also mentioned the ability

Dentistry 3000
Vol 11 No 1 (2023) DOI 10.5195/d3000.2023.380

of FGG to achieve complete root coverage in a one-stage procedure in 89.9% of sites [6]. However, postoperative pain and the long healing time required for the donor site are undesirable complications for both clinician and patient [7]. Traditional dressings are used as a physical barrier that protects wounds from oral environment without promoting cellular activities or biological sequence during the healing process [8]. Therefore, researchers have been interested in using natural substances, including turmeric and its extracts, as dressings to reduce postoperative pain and inflammation [9].

Turmeric belongs to the Zingiberaceae family of plants. It is native to tropical Asia [10]. It consists of a group of three curcuminoids: Curcumin (77%), Demetossicurcumin (17%), and Bisdemetossicurcumina (6%) [11]. Curcuminoids are known as phenolic compounds that have shown a great variety of biological functions, such as: antioxidant, anti-inflammatory, antimicrobial, and anti-cancer effects [12]. Consequently, there has been an increasing interest in curcuminoids due to their medicinal use. However, the Curcuminoids have a weak pharmacokinetics, such as its low plasma concentration, limited tissue distribution, high rate of metabolism and rapid systematic clearance [10, 13, 14], especially the orally administered form [14]. This has underlined the need for modifications to current formulations [13].

Many studies evaluated the safety of the Curcuminoids [14] and they have concluded that standardized powder and extract forms of turmeric and curcuminoids are safe for human use, even at high doses. Turmeric is considered a GRAS (Generally Recognized as Safe) by the U.S. Food and Drug Administration (FDA) [16].

Baum's study showed that the oral intake of 1 - 4 g/day of curcuminoids for 6 months was bioavailable and did not show any major toxicity or severe adverse effects [15].

In periodontal surgery, curcuminoids have been used in adjunctive therapy along with the mechanical phase to treat gingivitis and periodontitis and that is due to their anti-inflammatory properties as well as their ability to accelerate the healing process [9, 17, 18]. such substance has also been used on aphthous lesions and lichen planus, as it possesses analgesic effect [19].

This study aimed to compare the therapeutic effects of an oral gel prepared from a dried ethanolic turmeric extract with a 10% concentration comparing to the conventional gingival dressing (COE-PAK) on the donor site following gingival grafting procedures.

Material and Methods

Study Design

This study was a 2-arm, parallel-group, randomized controlled clinical trial with a 1:1 allocation ratio. The research gel obtained approval from the Ethical Committee of Damascus University, Syria (No 471/m - 12/5/2021). This study received approval from the Institutional Review Board (IRB) of Damascus University (No 3150 - 7/9/2020). This study was registered at the ISRCTN database (Identifier: ISRCTN14159005), and it was funded by Damascus University, postgraduate research budget (Ref: 88032002507DEN).

Sample Size Calculation

A pilot study was conducted on 8 patients to determine the sample size. Based on the pilot study results the effect size was 1,73 (standard deviation = 0,57); the sample size was calculated using G.power 3.1.9.2 program with 95% power at the 5% significance level, the confidence level was determined by 95% and two independent means as the statistical test. The number of the study sample was 20 patients, but to avoid any dropouts which may occur during the study, the number of patients was increased to 22 participants. The sample size was determined based on the null hypothesis, which states that the 10% turmeric gel has no effect on the healing and re-epithelialization of the donor site for free gingival graft and reduces postoperative pain.

Dentistry 3000
Vol 11 No 1 (2023) DOI 10.5195/d3000.2023.380

Participants, Eligibility Criteria, and Setting

Twenty-two patients were included in this study. The patients were recruited from the Periodontology Department at Damascus University in Syria between August and December 2021. The inclusion criteria in this study were the following: patients 18 years of age or older, good oral hygiene, no systematic disease, and have less than 1 mm attached gingiva width in the mandibular anterior region. The exclusion criteria were: pregnant or lactating women, smokers, patients undergoing active orthodontic treatment, gingival or periodontal diseases, systemic conditions, uncontrolled plaque accumulation, or those taking medications that impede the healing process. The surgical procedure, benefits, and possible side effects were explained to all patients, and written informed consent was obtained.

Randomization and allocation concealment.

Patients were randomly distributed into 2 groups: group I (was treated with 10% turmeric gel), or group II (was treated with non-eugenol gingival dressing). The allocation sequence (allocation ratio of 1:1) was done using a box containing 22 opaque sealed envelopes, eleven of which were containing a piece of paper identified with "control group" and eleven were containing a piece of paper marked with "experiment group". each patient was instructed to choose one envelop from the box; the patient was put into one of the two groups based on their chosen envelop. the envelope was opened immediately at the end of the surgical procedure. Follow-up measurements were done by another clinician who was blind to the current study.

Interventions

In the experimental group, donor sites were treated with 10% Curcuma longa extract gel following the surgical procedure of FGG, whereas the control group was treated using non-eugenol periodontal dressing (Coe-Pak).

Turmeric Extract Preparation

The whole turmeric plants were obtained from the local market. the botanical classification was done at the department of pharmacognosy at Faculty of Pharmacy, Damascus University; then Turmeric rhizomes washed, and air-dried for one week. Turmeric roots were manually crushed, smashed into little pieces to increase the extraction outcome, and then soaked in 100% ethanol with a proportion of 1:20 at ambient temperature for 72 hours. The extraction liquid was filtered using a filter paper then the liquid was desiccated using a rotary evaporator at 50^{o} C until the ethanol was vaporized. The calibration for curcuminoids was done by a team of pharmacists from Damascus University by using High-performance Thin Layer Chromatography (HPTLC), and it was between a range from 4-6% similar to other studies [42,43]

Gel Preparation

Every 100 grams (g) of turmeric gel contains 10 (g) of dried ethanolic turmeric extract which was added to 3 g of 24-hour-soaked Carbopol 934, then 3 milliliters (mL) of triethanolamine and 70 mL of polyethylene glycol 400 were added, with the help of an electric stirrer, then 0.02 g of Ethylenediamine tetraacetic acid (EDTA), 0.02 g methylparaben, and 0.18 g propylparaben were added to the mixture. Finally, Sorbitol 70% was added to refine the taste. The Components were weighed by an electronic scale (Precisa company/ UK). Sterilization was done by 25-kilo grays of gamma-ray at the Atomic Energy Commission of Syria.

Gel Administration

Group I patients were instructed to apply a thin layer of the turmeric gel four times per day and wear the stent and avoid eating and drinking for 30 minutes to allow the concentration of curcuminoids to increase to a level of clinical manifestation.

Pre-Surgical Procedures

Intra-oral examination and periodontal evaluation were conducted for each patient. All patients underwent mechanical periodontal treatment and received

Dentistry 3000
Vol 11 No 1 (2023) DOI 10.5195/d3000.2023.380

oral hygiene instructions. After 2 weeks, oral hygiene and periodontal health were re-evaluated. Only patients with good compliance were included. A maxillary alginate impression was taken during the same re-evaluation session to fabricate a 1-mm acrylic stent for post-operative use in order to hold the materials in close contact with the surgical site.

The Surgical Procedure

Patients in both groups underwent the same surgical procedures. Local anesthesia was administrated in both donor and recipient sites using 2% Lidocaine with 1:80,000 Epinephrine. The recipient site was prepared by performing a horizontal incision along the mucogingival line and two vertical releasing incisions were made from the lateral ends of the horizontal incision to the alveolar mucosa. A split-thickness flap was made without disturbing the underlying periosteum, and the flap was made with sufficient depth to avoid graft movement. The recipient site was rinsed with saline and covered with saline-moistened gauze until the graft was transferred. A #15 surgical blade was used to harvest the graft from the palate, between the distal aspects of the canines and the first molars, leaving 3 mm of undisturbed tissue from the gingival margin. After harvesting the graft, a saline-moistened gauze was applied to the palatal site to achieve hemostasis. The graft was immediately transferred to the recipient site and secured to the adjacent intact attached gingiva using two 5-0 nylon sutures. Furthermore, a periosteal suture was used to stabilize the graft without penetrating it.

Gentle pressure was applied for two minutes on the graft with a saline-moistened gauze. Care was taken to avoid mobilizing the graft as to not impede the healing process. The periodontal dressing was used in donor and recipient sites in the control group (group II) (Figure 1).

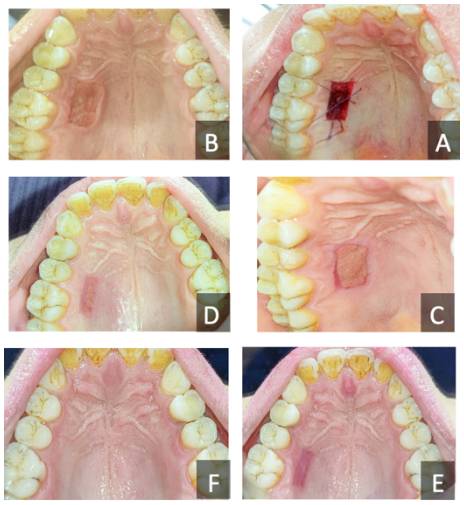

Figure 1. *Palatal wound healing for Group II: (A) Day 0, (B) Day 7, (C) Day 14, (D) Day 21, (E) Day 28, and (F) after two months*

In the experimental group (group I), patients were treated with 10% turmeric extract gel which was applied to donor and recipient sites and Patients were instructed to apply the gel four times per day for 14 days (Figure 2).

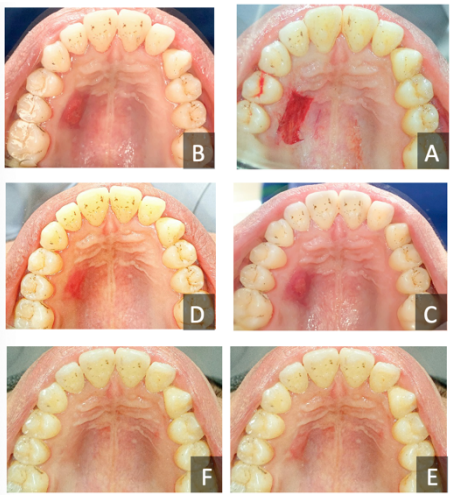

Figure 2. *Palatal wound healing for Group I: (A) Day 0, (B) Day 7, (C) Day 14, (D) Day 21, (E) Day 28, and (F) after two months*

Post-surgical care

Diclofenac potassium 50 mg Tablets (Cataflam, Novartis®) were described only if needed and patients were instructed to count the number of pills taken for indirect pain measurement via mean consumption of analgesics. Patients were recommended to follow a soft diet and to avoid brushing and flossing in the surgical area for 14 days, after which sutures were removed. A 0.12% chlorhexidine rinse was prescribed twice daily to limit bacterial growth. photographs were taken for the palatal wound on day 7, 14, 21, 28, and finally after two months, after surgery for evaluation of the healing of the palatal wound.

Outcomes

The Primary Outcome

Pain Level via VAS: patients were asked to record palatal pain values every day for the first 7 days

Dentistry 3000
Vol 11 No 1 (2023) DOI 10.5195/d3000.2023.380

according to the Visual Analogue Scale (VAS) of Yale University, which defines 0 as no pain and 10 as extreme pain [20].

Consumption of Analgesics: The indirect assessment for pain index was done by mean consumption of analgesics for 7 days after surgery, recorded in milligrams [21].

The Secondary Outcome

The wound healing index: This index evaluates healing process based on bleeding, pus, redness, granulation formation, and the amount of exposed connective tissue. Healing assessments were done once per week for a total of 4 assessments and were based on a scale of 1 (very poor) to 5 (excellent) healing [22].

Color Match Index: The color of the palatal wound was evaluated by comparing it with the palatal mucosa of the opposite side by using the objective VAS of Yale University. Where 0 indicates no color match and 10 indicates an excellent color match with the adjacent tissues. The assessment process was done on day 7, day 14, day 21, day 28, and after 2 months [23].

Re-epithelization Index: using 1% Toluidine Blue, was applied to the donor site every week for the first four weeks following surgery. The navy-blue staining was considered incomplete epithelization, whereas light blue staining was considered complete epithelization. Results were graded on a scale of I to III, where (I) is re-epithelialization of less than half of the Surgical site, (II) is re-epithelialization of more than half of the Surgical site, and (III) is complete re-epithelialization [24].

Wound Size Index*:* Wound size was measured vía periodontal Pobre (UNC 15). a transparent film was placed on the wound area, and the margin of the wound was traced with a pen, then the length and width of the wound were meagered using UNC-15 probe. The measuring process was done on surgery day and days 7, 14, 21, and 28 [25].

Statistical Analysis

The statistical data analysis was performed using SPSS software version 25.0 (SPSS, Inc., Chicago, USA). The statistical significance level was determined at $p<0.05$. Mann-Whitney U was applied for the healing index, the Independent Samples Test was used to compare mean differences between the two groups in terms of VAS for pain level, analgesic consumption, color match, and wound size index, and Chi-Square for the Re-epithelization index.

Results

CONSORT guideline shows the flow and distribution of the participants (Figure 3). A total of 22 patients (6 males, 16 females) were included in the study and divided into two groups of 11 participants. During the follow-up phase, 2 patients were lost (one patient from each group). The statistical analysis was only applied to patients who were present for both the examination and the follow-up.

Group I consisted of 80% female and 20% male, while group II was 70% female and 30% male with no statistical difference. The age of patients ranged between 20 and 52 years of age. The mean age was 38 ± 8.95 for group I and 37 ±9.39 for group II with no statistical difference.

Dentistry 3000
Vol 11 No 1 (2023) DOI 10.5195/d3000.2023.380

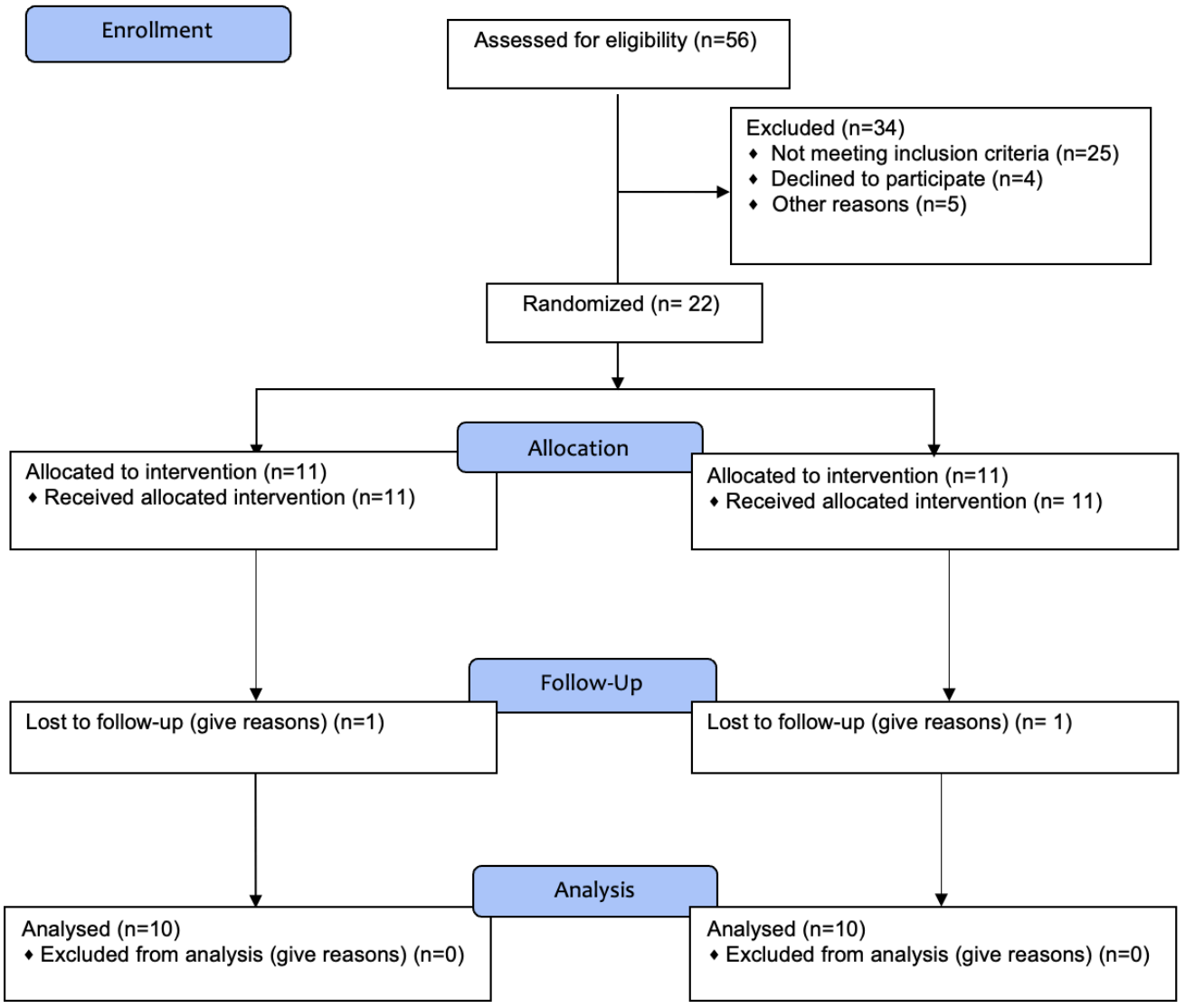

Figure 3. *CONSORT flow diagram.*

The Primary Outcome

Pain level via VAS: The mean of VAS values was significantly lower in group I than in group II on days 3-7 ($p<0.05$), whereas the difference was not significant on days 1 and 2, where the highest mean was recorded in group II ($p=0.112$ and $p=0.107$ respectively) (Table 1).

Postoperative Analgesic Consumption (in mg): On day 1, and 2 the highest median values for total analgesic consumption were recorded in group II; however, this difference did not reach the level of statistical significance. On days 3-7, there was a statistically significant difference, where the group I showed a noticeable reduction in analgesic consumption ($p<0.05$) (Table 2).

The Secondary Outcome

Wound Healing Index: Mean values were significantly higher in group I than in group II for the first week ($p=0.002$), and second week ($p=0.01$), whereas the difference was not significant in the third ($p=0.328$) and fourth weeks ($p=1$) (Table 3).

Color Match Index: There was a significant difference with higher

Dentistry 3000
Vol 11 No 1 (2023) DOI 10.5195/d3000.2023.380

matching in group 1 on day 7, 14, 21, and 28 where the highest median and range values were recorded in group I, compared to group II; however, there was no significant difference between the groups after two months where both groups recorded complete color matching (Table 4).

Re-epithelization index: There was no significant difference in the donor site re-epithelization between group I and II at any of the follow-up appointments ($p>0.05$). On week 1, re-epithelization appeared to be less than half of the Surgical site for both groups ($p=1$). On week 2, 60% of group I demonstrated re-epithelialization of more than half of the Surgical site, whereas only 40% was seen in group II. On week 3, complete re-epithelialization was seen in 50% of group I and 40% of group II. On week 4, complete palatal re-epithelization was seen in all patients ($p=1$) (Table 5).

Wound Size Index: The results of the study demonstrated that the difference between groups did not reach the level of statistical significance, although the highest mean value was recorded in group II at all of the follow-up periods (Table 6).

Discussion

Previous studies aimed to expedite the healing process through the use of many biological materials (A-PRF) [26], ozone therapy [27], hyaluronic acid [28], especially following mucogingival surgery. Since each material has its pros and cons, this study is fundamental in the search for the ideal material. This study is the first to use 10% turmeric extract gel in terms of the healing of second intention wounds. Such concentration is considered to be the maximum possible concentration in the gel form and is sufficient to show clinical results. On the other hand, Raghava et al, Meghana et al. and Jalaluddin et al studies have used 1% extract [9, 17, 18].

A large number of studies have revealed the benefits of turmeric extract as antioxidants [29] and anti-inflammatory agents [30]. However, very limited research is available to test turmeric's effectiveness in improving the healing process and reducing postoperative pain following mucogingival surgeries.

Turmeric extract has poor oral bioavailability and was therefore applied topically to the palatal surgical site.

Post-operative pain is considered a natural phenomenon. It gradually reduces as the healing progress [31]. Because postoperative pain of the donor site is associated with the wound depth rather than surface area, the thickness of the graft was standardized as 1-1.5 mm. Thicker grafts could cause necrosis as a result of ischemia, while a graft that is shallower would have a low resistance to functional forces [32].

Pain values were recorded daily for the first 7 postoperative days according to VAS values between 0 and 10. On days 1 and 2, there was no significant difference in the highest median of the VAS score in each group. Although the highest value for VAS pain score was noted in group II (Table 1). This could be due to the fact that the effectiveness of curcuminoids relies on their concentration in the wound site. This concentration may take multiple days to build up, hence the lack of difference in VAS score between groups I and II.

The range and mean values of the VAS score decreased significantly in group I on days 3 to 7 when compared to group II. This could be explained by the fact that curcuminoids reduce pain through several mechanisms: First, curcuminoids can prevent the synthesis of Prostaglandin E2 (PGE2) [33] which is an important mediator produced in injured nerves, and facilitate the synthesis of pain-related molecules [34]. Second, curcuminoids can stimulate corticosteroid secretion from the adrenal gland by inhibiting potassium channels (i.e. bTREK-1) and depleting neurotransmitter substances at the nerve endings [33]. Third, the curcumin molecule has a vanilloid moiety which causes the desensitization of the transient receptor potential cation channel (TRPV1) which plays a critical role in nociceptive neural detection and transmission [15].

Dentistry 3000
Vol 11 No 1 (2023) DOI 10.5195/d3000.2023.380

In this study pain index was measured both directly via VAS and indirectly via consumption of analgesics; thus patients were instructed to take Diclofenac potassium 50 mg orally only if needed. No other medications were prescribed even antibiotics. infections after mucogingival surgery usually are less than 5%, if the patient maintains good oral hygiene and this low-risk infection does not justify the preventive use of antibiotics. The maximum level of analgesic consumption was in the initial healing phase (first and second day) with no satistical difference between the study groups. Group I showed a dramatically significant decrease compared with group II in the amount of analgesic use from day 3 to day 7, and that reflects the powerful analgesic and anti-inflammatory effect of curcuminoids. Such a result agrees with the findings of the pain index measured via VAS score. Curcuminoids are characterized by having in addition to their anti-inflammatory effects, high tolerance and fewer side effects compared with noncorticosetiroid anti-inflammatory drugs, especially in long-term treatment [35]. Although all the criteria used to evaluate the pain level are subjective but it is the most wildly used for this purpose in other studies and it has proven a good efficiency in the evaluation result treatments [36].

The healing progress was recorded on days 7, 14, 21, and 28 following the surgery in accordance to the Landry, et al. index, which consists of 5 degrees.

Group I exhibited a significant difference in the rate of healing in weeks 1 and 2 when compared to group II ($p < 0.05$). This result can be explained by the results of the *In Vetro* study by Rujirachotiwat and Suttamanatwong which reveal the ability of curcumin in increasing the expression of RNA-m for growth factors (EGFR, KGF-1) and collagen type-1 gene (COL1) in term of healing [37]. Iova et al also demonstrated the antioxidant properties of curcumin, as it decreases the free radical damage in periodontal tissue which improves the healing process [38]. Since uncontrolled inflammation hinders the healing process, curcuminoids act through several mechanisms to modify the inflammatory process by disturbing the calcium channels in the cell membranes which play an important role in the activation of lymphocytes and inflammatory cells. Curcuminoids also reduce the number of molecules involved in inflammation such as Tumor necrosis factor-alpha (TNF-a), Interleukin-1 (IL-1), Cyclooxygenase-2 (COX-2), leukotrienes, nitric oxide, and lipoxygenase [29, 30].

Even though median values in group I were higher than in group II, our study showed that there is no statistical difference between the two groups on days 21 and 28 (Table 3). This can be explained that the gel was applied only for 14 days leading to a decrease in concentrations of the extract in the surgical site, in addition to the completion of the healing on day 28. No studies were found on the effect of curcumin or turmeric extract on the healing of intraoral secondary intention wounds.

The re-epithelialization test was scored at 1, 2, 3, and 4 weeks following surgery using 1% Toluidine Blue colorant. There was no statistical difference between both groups at any of the follow-up periods. It is worth noting that the percentage of re-epithelialization was higher in group I compared to group II in all of the Follow-up periods (Table 5).

Many studies have confirmed that epithelization was not complete during week 1 in (COE-PAK) groups [39] and complete epithelization was scored in the fourth week for all individuals [26, 40]. No studies were found on the effect of topical curcumin or turmeric extract on the re-epithelialization of intraoral surgical sites. Table 5 shows a higher percentage in the re-epithelialization area at all follow-up periods with no satistical difference for group I and that can be explained by the ability of curcuminoids to improve collagen deposition and accelerate the re-epithelialization [29] by stimulating the formation of transforming growth factor-beta (TGF-b) that accelerates angiogenesis and the remodeling process [41].

Color matching index: As healing of FGG takes place by secondary intention, the color change in donor

Dentistry 3000
Vol 11 No 1 (2023) DOI 10.5195/d3000.2023.380

site is observed. Color matching was assessed on day 7, day 14, day 21, day 28, and after 2 months via VAS. There is a significantly higher score in group I compared with group II in days 7, 14, 21, and 28. The color matching between the palatal donor site and the adjacent normal tissue would reflect the degree of re-epithelization and wound-healing so maybe the curcuminoids have an antiinflammatory effect more than accelerating the epithelial creeping of palatal wound.ace between the stud There is no statistical difference between the study groups after three months as all patients achieved a complete palatal color match.

Wound size was measured in this study by periodontal prob (UNC 15). The evaluation was taken on surgery day, the seventh day, the fourteenth day, the twenty-fist day, and the wenty-eighth day and that was when complete epithelial healing was recorded for all patients. All groups showed a significant reduction in wound size from day 0 to day 42; however, no significant difference between groups was detected in wound size in each time interval. The measuring process was only done on width and length which does not provide accurate measurement due to the irregular healing pattern of the wound.

There were no side effects observed on any patient in the experimental group.

Although more clinical studies are needed on turmeric extract in the field of dentistry and particularly in periodontology, this study has shown its effectiveness in accelerating surgical site healing, as well as postoperative pain control.

Table 1. Median and range VAS score for postoperative pain from day 1 to day 7.

Time		Median	range min - max		95% cl of the difference (lower bound - Upper bound)		P value
Day 1	Group (I)	5.6	5	8	-2.881	0.681	0.207 **
	Group (II)	7	5	9			
Day 2	Group (I)	5.3	4	8	-3.597	0.597	0.150 **
	Group (II)	6.8	4	10			
Day 3	Group (I)	3.7	2	7	-4.771	-1.829	0.000 *
	Group (II)	6,3	4	9			
Day 4	Group (I)	3.4	2	6	-5.043	-2.957	0.000 *
	Group (II)	5.9	3	8			
Day 5	Group (I)	3.2	2	6	-5.262	-2.338	0.000 *
	Group (II)	5,7	5	8			
Day 6	Group (I)	2.8	1	6	-5.445	-2.955	0.000 *
	Group (II)	5,2	3	8			
Day7	Group (I)	1.9	0	5	-5.201	-2.599	0.000 *
	Group (II)	4.8	1	7			

Significance level: $p \leq 0.05$; * = significant; ** = nonsignificant.

Dentistry 3000
Vol 11 No 1 (2023) DOI 10.5195/d3000.2023.380

Table 2. Median and range values of analgesic consumption (mg) daily.

Time		Median	Min	Max	95% cl of the difference (lower bound - Upper bound)		P value
Day 1	Group (I)	160	2	4	-1.200	0.600	0.492 **
	Group (II)	180	3	4			
Day 2	Group (I)	150	2	4	-1.174	0.374	0.292 **
	Group (II)	165	3	4			
Day 3	Group (I)	100	1	3	-1.860	-0140	0.021 *
	Group (II)	150	2	4			
Day 4	Group (I)	80	1	3	-2.273	-0.320	0.012 *
	Group (II)	145	2	3			
Day 5	Group (I)	80	0	3	-2.400	-0.400	0.009 *
	Group (II)	120	1	3			
Day 6	Group (I)	50	0	2	-1.755	-0.045	0.040 *
	Group (II)	105	1	2			
Day7	Group (I)	45	0	2	-1.993	0.350	0.037 *
	Group (II)	95	0	2			

Significance level: $p \leq 0.05$; * = significant; ** = nonsignificant.

Table 3. Median score for healing index.

Time		Median	P value
Week 1	Group (I)	2.4	0.002 *
	Group (II)	1.4	
Week 2	Group (I)	3.6	0.01 *
	Group (II)	2.8	
Week 3	Group (I)	4.6	0.328 **
	Group (II)	4.3	
Week 4	Group (I)	5	1 **
	Group (II)	4.9	

Significance level: $p \leq 0.05$; * = significant; ** = nonsignificant.

Dentistry 3000
Vol 11 No 1 (2023) DOI 10.5195/d3000.2023.380

Table 4. Median and range values of color match measured by the Visual Analogue Scale score.

Time		Median	Min	Max	P value
Week 1	Group (I)	3.3	2	5	0.041 *
	Group (II)	1.5	0	4	
Week 2	Group (I)	4.8	3	6	0.037 *
	Group (II)	3.2	2	5	
Week 3	Group (I)	6.9	5	8	0.032 *
	Group (II)	5.1	4	7	
Week 4	Group (I)	8.1	6	10	0.047 *
	Group (II)	6.9	5	9	
After 2 months	Group (I)	10	10	10	0.660 **
	Group (II)	10	10	10	

Significance level: p ≤ 0.05; * = significant; ** = nonsignificant.

Table 5. Median and percentage of re-epithelialization from week 1 to week 4.

Time		Grades	Percentage	P value
Week 1	Group (I)	G (I)	100%	1 **
	Group (II)	G (I)	100%	
Week 2	Group (I)	G (I)	40%	0.65 **
		G (II)	60%	
	Group (II)	G (I)	60%	
		G (II)	40%	
Week 3	Group (I)	G (II)	50%	0.074 **
		G (III)	50%	
	Group (II)	G (II)	60%	
		G (III)	40%	
Week 4	Group (I)	G (III)	100%	1 **
	Group (II)	G (III)	100%	

G (I): re-epithelialization of less than 50% of the wound area
G(II): re-epithelialization of more than 50% of the wound area
G (III): complete re-epithelialization
Significance level: p ≤ 0.05; * = significant; ** = nonsignificant.

Table 6. Mean values for the wound size index (mm) at all time points.

Time		Mean	Std. dev.	Std. error	95% cl of the difference (lower bound - Upper bound)		P value
Day 0	Group (I)	132.0	32.46	9.23	117.53	151.37	1 **
	Group (II)	125.0	36.62	9.73	98.83	150.36	

Dentistry 3000
Vol 11 No 1 (2023) DOI 10.5195/d3000.2023.380

Day 7	Group (I)	102.4	37.21	8.34	97.48	135.24	0.227 **
	Group (II)	108.7	35.78	8.41	84.95	134.62	
Day 14	Group (I)	82.5	29.72	10.84	74.38	117.41	0.06 **
	Group (II)	88.3	33.67	9.19	68.46	114.73	
Day 21	Group (I)	65.6	31.84	10.51	56.27	93.18	0.782 **
	Group (II)	74.9	34.54	9.39	53.92	91.48	
Day 28	Group (I)	49.7	33.63	8.46	35.61	67.52	0.595 **
	Group (II)	57.2	35,27	8.52	32,74	63.83	

Significance level: p ≤ 0.05; * = significant; ** = nonsignificant.

Conclusion

Topical application of 10% Curcuma longa extract gel on palatal wound following FGG harvesting could effectively promote palatal wound healing index. In addition to reducing postoperative pain, it improves the color match index for donor site following FGG harvesting, thereby 10% turmeric extract gel is a viable alternative to traditional gingival dressing (COE-PAK), as it is easily applied and haas better biological effects.

References

1. *Surgical techniques to increase the apicocoronal dimension of the attached gingiva: a 1-year comparison between the free gingival graft and the modified apically repositioned flap.* Carnio, J., P.M. Camargo, and P.Q. Pirih. Int J Periodontics Restorative Dent, 2015. 35(4): p. 571-8.
2. *Clinical and histological evaluation of two dressing materials in the healing of palatal wounds.* Shanmugam, M., et al. Journal of Indian Society of Periodontology, 2010. 14(4): p. 241.
3. *Free transplantation of gingival propria.* Bjorn, H. Odontol Revy, 1963. 14: p. 323.
4. *Dimensional changes in free gingival grafts: scalpel versus Er: YAG laser—a preliminary study.* Türer, Ç.C., et al. Lasers in medical science, 2015. 30(2): p. 543-548.
5. *Root coverage grafting for regeneration and aesthetics.* MILLER JR, P.D. Periodontology 2000, 1993. 1(1): p. 118-127.
6. *Root coverage using the free soft tissue autograft following citric acid application. III. A successful and predictalbe procedure in areas of deep-wide recession.* Miller Jr, P. Int. J. Periodont. Rest. Dent, 1985. 5: p. 14-36.
7. *Postoperative complications following gingival augmentation procedures.* Griffin, T.J., et al. Journal of periodontology, 2006. 77(12): p. 2070-2079.
8. *Effect of Propolis Extract in Combination with Eugenol-Free Dressing (Coe-PakTM) on Pain and Wound Healing after Crown-Lengthening: A Randomized Clinical Trial.* Askari, M., et al. Journal of Dentistry, 2017. 18(3): p. 173.
9. *Comparison of effect of curcumin gel and noneugenol periodontal dressing in tissue response, early wound healing, and pain assessment following periodontal flap surgery in chronic periodontitis patients.* Meghana, M.V.S., et al. Journal of Indian Society of Periodontology, 2020. 24(1): p. 54.
10. *Curcumin: Biological, pharmaceutical, nutraceutical, and analytical aspects.* Kotha, R.R. and D.L. Luthria. Molecules, 2019. 24(16): p. 2930.
11. *Safety and efficacy of turmeric extract, turmeric oil, turmeric oleoresin and turmeric tincture from Curcuma longa L. rhizome when used as sensory additives in feed for all animal species.*

Dentistry 3000
Vol 11 No 1 (2023) DOI 10.5195/d3000.2023.380

Additives, E.P.o., et al. EFSA Journal, 2020. 18(6): p. e06146.

12. *Therapeutic effects of turmeric in several diseases: An overview.* Hay, E., et al. Chemico-biological interactions, 2019. 310 :p. 108729.
13. *Bioavailability of curcumin: problems and promises.* Anand, P., et al. Molecular pharmaceutics, 2007. 4(6): p. 807-818.
14. *Turmeric (Curcuma longa) and its major constituent (curcumin) as nontoxic and safe substances.* Soleimani, V., A. Sahebkar, and H. Hosseinzadeh. Phytotherapy Research, 2018. 32(6): p. 985-995.
15. "Six-month randomized, placebo-controlled, double-blind, pilot clinical trial of curcumin in patients with Alzheimer disease." Baum, Larry, et al. Journal of clinical psychopharmacology 28.1 (2008): 110-113.
16. *Safety evaluation of certain food additives and contaminants*. Organization, W.H. Vol. 68. 2008: World Health Organization.
17. *Efficacy of Curcumin as an Adjunct to Scaling and Root Planing in Chronic Periodontitis Patients: A Randomized Controlled Clinical Trial.* Raghava, K.V., et al. The journal of contemporary dental practice, 2019. 20(7): p. 842-846.
18. *Antimicrobial activity of Curcuma longa L. extract on periodontal pathogens.* Jalaluddin, M., et al. Journal of pharmacy & bioallied sciences, 2019. 11(Suppl 2): p. S203.
19. *Curcumin, a turmeric extract, for oral lichen planus: A systematic review.* White, C.M ,.K. Chamberlin, and E. Eisenberg. Oral diseases, 2019. 25(3): p. 720-725.
20. *The clinical evaluation of the effects of low-level laser therapy on the donor and recipient sites of the free gingival graft: a case series.* Lafzi, A., et al. Journal of Lasers in Medical Sciences, 2019. 10(4): p. 355.
21. *Patient morbidity and root coverage outcome after subepithelial connective tissue and de-epithelialized grafts: a comparative randomized-controlled clinical trial.* Zucchelli, G., et al. Journal of clinical periodontology, 2010. 37(8): p. 728-738.
22. *The clinical evaluation of platelet-rich plasma on free gingival graft's donor site wound healing.* Samani, M.K., et al. European Journal of Dentistry, 2017. 11(04): p. 447-454.
23. *Effect of topically applied hyaluronic acid on pain and palatal epithelial wound healing: An examiner-masked, randomized, controlled clinical trial.* Yıldırım, S., et al. Journal of periodontology, 2018. 89 :(1)p. 36-45.
24. *Toluidine blue: A review of its chemistry and clinical utility.* Sridharan, G. and A.A. Shankar. Journal of oral and maxillofacial pathology: JOMFP, 2012. 16(2): p. 251.
25. *Contents: MEASURE: A proposed assessment framework for developing best practice recommendations for wound assessment.* Keast, D.H., et al. Wound Repair and Regeneration, 2004. 12: p. s1-s17.
26. *Effect of A-PRF application on palatal wound healing after free gingival graft harvesting: a prospective randomized study.* Sousa, F., et al. European Journal of Dentistry, 2020. 14(01): p. 063-069.
27. *Effects of laser photobiomodulation and ozone therapy on palatal epithelial wound healing and patient morbidity.* Isler, S.C., et al. Photomedicine and Laser Surgery, 2018. 36 :(11)p. 571-580.
28. *Clinical Comparison of MEBO and Hyaluronic Acid Gel in the Management of Pain after Free Gingival Graft Harvesting: A Randomized Clinical Trial.* Hassan, A., et al. International Journal of Dentistry, 2021. 2021.
29. *Curcumin as a wound healing agent.* Akbik, D., et al. Life sciences, 2014. 116(1): p. 1-7.
30. *Efficacy of turmeric extracts and curcumin for alleviating the symptoms of joint arthritis: a systematic review and meta-analysis of randomized clinical trials.* Daily, J.W., M. Yang, and S. Park. Journal of medicinal food, 2016. 19(8): p. 717-729.
31. *Post–Operative complications of periodontal surgery.* Kirmani, M., et al. Int J Contemp Med Res, 2016. 3: p. 1285-6.
32. *Periodontal soft tissue non–root coverage procedures: A consensus report from the AAP Regeneration Workshop.* Scheyer, E.T., et al. Journal of periodontology, 2015. 86: p. S73-S76.
33. *Curcumin treatment attenuates pain and enhances functional recovery after incision.* Sahbaie, P., et al. Anesthesia & Analgesia , :(6)118 .2014p. 1336-1344.
34. *Does COX2-dependent PGE2 play a role in neuropathic pain?* Ma, W. and R. Quirion. Neuroscience letters, 2008. 437(3): p. 165-169.
35. *Analgesic efficacy and safety of curcuminoids in clinical practice: a systematic review and meta-*

Dentistry 3000
Vol 11 No 1 (2023) DOI 10.5195/d3000.2023.380

analysis of randomized controlled trials. Sahebkar, A. and Y. Henrotin. Pain medicine, 2016. 17(6): p. 1192-1202.

36. *Concordance among different pain scales in patients with dental pain.* dos Santos Calderon, P., et al. Journal of orofacial pain :(2)26 .2012 ,p. 126.
37. *Curcumin promotes collagen type I, keratinocyte growth factor-1, and epidermal growth factor receptor expressions in the in vitro wound healing model of human gingival fibroblasts.* Rujirachotiwat, A. and S. Suttamanatwong. European Journal of Dentistry, 2021. 15(01): p. 063-070.
38. *The antioxidant effect of curcumin and rutin on oxidative stress biomarkers in experimentally induced periodontitis in hyperglycemic Wistar rats.* Iova, G.M., et al. Molecules, 2021. 26(5): p. 1332.
39. *Clinical comparison of platelet-rich fibrin and a gelatin sponge in the management of palatal wounds after epithelialized free gingival graft harvest: A randomized clinical trial.* Femminella, B., et al. Journal of periodontology, 2016. 87(2): p. 103-11.3
40. *Clinical study of laser biomodulation (650λ) after free gingival grafts.* Vieira, J., et al. J Oral Laser Appl, 2010. 10: p. 159-63.
41. *A review of therapeutic potentials of turmeric (Curcuma longa) and its active constituent, curcumin, on inflammatory disorders, pain, and their related patents.* Razavi, B.M., M. Ghasemzadeh Rahbardar, and H. Hosseinzadeh. Phytotherapy Research, 2021. 35(12): p. 6489-6513.
42. Hydrotropic extraction of curcuminoids from turmeric. Dandekar DV, Gaikar V. Separation science and technology. 2003;38(5):1185-1215.
43. Extraction and purification of curcuminoids from Turmeric (Curcuma longa L.). Kulkarni S, Maske K, Budre M, Mahajan R. International Journal of Pharmacology and Pharmaceutical Technology. 2012;1(2):81-84.