Original Article

An evaluation of the efficacy of ethanolic extract of *Nigella sativa* L. (*Kalonji*) on the clinical parameters of moderate-to-severe gingivitis: A split-mouth clinical study

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Abstract

Introduction: Gingivitis is a relatively innocuous and reversible inflammation of gingiva. If left untreated, it might progress involving the deeper supporting periodontal tissues of the tooth with consequent mobility and tooth loss. Compelling literature has suggested the role of local antibacterial and anti-inflammatory agents as an adjunct to scaling and root planing (gold standard) for treating periodontal diseases. Various herbs such as *Nimba* (*Azadirachta indica* A. Juss), *Babbula* (*Vachellia nilotica* (L.) P.J.H. Hurter & Mabb.) and turmeric (*Curcuma longa* L.) have been used for gingivitis since ancient times. *Nigella sativa* L. (*Kalonji*) is one such herb known for its remarkable anti-inflammatory, antioxidant and antimicrobial properties and thus has been utilized in the present study. **Aim:** The aim of the study was to explore the clinical efficacy of different ethanolic solutions of *N. sativa* in moderate-to-severe gingivitis patients. **Materials and Methods:** It is a split-mouth clinical study with 24 patients of moderate-to-severe gingivitis from the age group of 25–45 years. Recruited individuals were divided in to group I_1, group II_1 and group III_1 (scaling and root planning i.e., control) and group I_2, group II_2 and group III_2 (experimental). Three doses of solution 1 (1:3), solution 2 (1:1) and solution 3 (3:1) were administered to the experimental groups for 3 consecutive days. The clinical parameters, i.e., gingival index (GI) and plaque index (PI) were recorded at baseline, 14 days and 28 days in all the individuals. ANOVA test was used in the study for statistical analysis. **Results:** Intergroup comparison in terms of GI showed statistically significant difference at 14th and 28th day from baseline between I_1 & I_2, at only 28th day between II_1 & II_2 and insignificant difference between III_1 & III_2 at all time intervals from baseline. On intragroup comparison, statistically significant reduction in GI in all groups from baseline till 28 days was found, but among experimental groups best result was seen in group III_2 ($P < 0.001$; F value 153.75). As far as PI is concerned, intergroup comparison between different groups displayed statistically significant difference from baseline to 14th and 28th day between all groups i.e I_1& I_2, II_1& II_2 and III_1& III_2. On intragroup comparison, statistically significant reduction in PI in all control groups i.e I_1, II_1 & III_1 was found, but among experimental groups only group III_2 provided statistically significant reduction ($P < 0.001$, F value 30.40). **Conclusion:** The results of this study indicate that, the ethanolic extract of *N. sativa* is effective in the treatment of moderate to severe gingivitis.

Keywords: Anti-inflammatory, clinical study, gingivitis, *Nigella sativa* (*Kalonji*), split-mouth

Introduction

The alarming emergence of drug resistance is known worldwide and it has provoked the researchers to find new, comparatively less expensive medicinally active compounds. The medicinal plants indigenous to their regions can be effectively utilized for the cure of diseases. Moreover, herbal medicines have an added benefit over modern allopathic medicine of being biologically safe.

Nigella sativa L. (*Kalonji*) is a miraculous herb with a rich historical and religious background. Commonly known as "blackseed", *Nigella sativa* is native to South-west Asia, Southern Europe and North Africa. Further, in Unani and Ayurveda[1,2] it holds an important place. It is a flowering plant

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belonging to the family of *Ranunculaceae*. In ancient times, Egyptian and Greek physicians utilized this miraculous herb for managing various diseases such as toothache, intestinal worms and headache.[3,4] *Nigella sativa* has a wide array of biological active compounds such as thymoquinone (TQ), dithymoquinone, thymol and thymo-hydroquinone. It can be effectively utilized as antihypertensive, antidiabetic, anticancer, diuretic, analgesic, anti-inflammatory, antimalarial, antimicrobial, spasmolytic, bronchio-dilator, gastro-protective, renal protective, hepato-protective, antioxidant and for neuropsychiatric diseases.[5-10]

Oral health is of prime importance to the general well-being of an individual. For many years, many herbal plants such as *Nimba* (*Azadirachta indica* A. Juss), *Aloe vera (Aloe barbadensis miller.)* and turmeric (*Curcuma longa* L.) have been used for preventing many oral ailments such as caries, oral ulcers, gingivitis and fungal infections. Studies relating *N. sativa* to oral health are scanty, and therefore, it has prompted the authors to utilize this wonder herb for improving oral health.

Gingivitis is the multifactorial microbial inflammatory disease affecting the gingiva surrounding the neck of tooth. If left untreated, it can result in the destruction of connective tissue and alveolar bone and consecutively loosening and loss of teeth. The periodontal treatment of tenin corporates the use of systemic and topical antibacterial agents. *N. sativa* also called as black cumin is one such herbal plant containing numerous active constituents. Among which, TQ is known for its remarkable anti-inflammatory and anti-oxidative properties and has shown an important role in preventing periodontal diseases.[11] A study on rat model has shown a significant improvement in periodontal indices, reduced sub-gingival bacterial counts, and preventing dental caries initiation when treated with TQ in drinking water or oral gel.[12]

Another morphometric and histopathological study has emphasized the preventive effect of TQ in initiation and progression of periodontal inflammation.[11] Further, an *in-vivo* study has also demonstrated the use of TQ chips delivered in the periodontal pockets of chronic periodontitis patients with significant gains in clinical attachments in TQ groups.[6] Further, an *in-vitro* study has shown the anti-bacterial effect of methanolic extracts of *N. sativa* against four bacterial isolates, i.e., *Escherichiacoli, Staphylococcuss, Pseudomonassyringa,* and *Bacillussubtilis*.[13]

Only a few *in-vitro* and animal studies have been reported in literature highlighting the protective role of *N. sativa* from periodontal disease point of view. Owing to its antibacterial, anti-inflammatory, and anti-oxidative properties, the authors believe that *N. sativa* could have a role in preventing periodontal inflammation. Some studies have also revealed that medicinal herbs have been actively working to improve the oral health by beneficial procedures such as *Kavala* (gargling) and *Gandusha* (holding of medicinal liquids in the mouth for some time). One of the study that has utilized turmeric gel has shown plaque index (PI) reduction of 60.81%and 60.21%whereas GI reduction of 71.79% and 71.20% at 0 and 21 days respectively.[14]Another study has used curcuma gel for evaluating its clinical efficacy on gingivitis by reducing its inflammatory causing components (Pearson's correlation ratio for preoperative [2.1910] and postoperative [1.2550] readings).[15]

Objectives

The objective of the present study is first to explore the clinical efficacy of different ratios of topically applied ethanolic solution of *N. sativa* (1:3, 1:1 and 3:1) on inflamed gingiva of moderate-to-severe gingivitis patients at baseline, 14thday and 28thday. Second, it will help in assessment of which ratio of the solution has a better clinical efficacy in the form of anti-inflammatory and antiplaque action and whether there are any associated adverse effects or not.

Materials and Methods

In the present split-mouth clinical study, a total number of 24 patients of moderate-to-severe gingivitis from the age group of 25–45 years were recruited from the Outpatient Department of Periodontology, Faculty of Dental Sciences, King George's Medical University (K.G.M.U) Lucknow. The different ratios of ethanolic extract of *N. sativa* were prepared in the National Botanical Research Institute, Lucknow. The ethical clearance was obtained by Institutional Ethics Committee, King George's Medical University, U.P (ECR/262/Inst/UP/2013/RR-19) 70/Ethics/2020.

Study designs

Selection and description of participants: Only those patients that had moderate to severe gingivitis to fulfil the split mouth design were randomly divided into three groups as per the inclusion and exclusion criteria with each group having 8 individuals. Computer assisted randomization was done with allocation concealment using opaque envelopes. All the individuals have given written consent prior to commencement of the trial.

Inclusion criteria

Systemically healthy patients, patients having moderate-to-severe gingivitis involving maxillary or mandibular incisors, who can be included insplit-mouth design (LoeandSilness; 1963) fulfilling the criteria of index 2 and 3 with only the facial surface of the maxillary and mandibular anterior teeth and patients who have not undergone periodontal therapy for the past 6 months were included.

Exclusion criteria

Patients with acute oral infections or chewing (arecanut and tobacco) or smoking habits or patients on any antibiotic therapy for the past 6 months or pregnant and lactating women were excluded from the present clinical trial.

Clinical parameters

The following clinical parameters were recorded at baseline, 14 days and 28 days in all the patients

1. GI- Gingival Index (LoeandSilness; 1963)
2. PI - Plaque Index (SilnessandLoe; 1964).

Isolation and preparation of *Kalonji* solution

Plant material

The seeds of *N.sativa* were purchased during August 2015 from local market of Lucknow, Uttar Pradesh, India. The samples were authenticated by the plant taxonomists at the CSIR-National Botanical Research Institute, Lucknow, India.

Extraction

The plant material *N. sativa* was (100 g) extracted with ethanol (800 mL × 4 times) in an extractor for 36 h by the maceration. The extract was filtered through Whatman filter paper and evaporated to dryness using rotatory evaporator (Buchi Rotavapor-R2, Flawil, Switzerland) under reduced pressure at 45°C. Dried residues were stored in vials at 4°C in the refrigerator for further use.

Dose preparation

Ethanolic extract of *N. sativa* was used for dose preparation along with glycerin as a carrier. Three doses were prepared along with carrier in different ratios and coded as solution 1 (1:3), solution 2 (1:1) and solution 3 (3:1).In the assay, glycerin was used as vehicle control.

Group allocation

The 24 patients recruited in the study fulfilling the inclusion criteria were randomly divided into the following groups depending on the solution used. The split-mouth design was taken in to account. Further randomization into experimental and control sites was done.

- GroupI_1: Patients subjected to scaling and root planing (SRP)
- GroupI_2: Patients in which *Kalonji* solution (solution 1) was applied topically on the surface of gingiva and gingival sulcus was irrigated with the same solution
- GroupII_1: Patients subjected to SRP
- GroupII_2: Patients in which *Kalonji* solution (solution 2) was applied topically on the surface of gingiva and gingival sulcus was irrigated with the same solution
- GroupIII_1: Patients subjected to SRP
- GroupIII_2: Patients in which *Kalonji* solution (solution 3) was applied topically on the surface of gingiva and gingival sulcus was irrigated with the same solution
- GroupI_1, groupII_1 and groupIII_1were considered as control groups where as groupI_2, groupII_2, and groupIII_2 to be experimental groups. Representative figures show the group allocation [Figures 1-3].

Methodology

Recording of all the clinical parameters was done before the start of the treatment (0 day). For group I_1, group II_1 and group III_1 (control group) patients, scaling was performed by ultrasonic scaler and meticulous root planning by hand instruments, for example, Gracey curettes until glossy hard surface was attained. The procedure was performed in such a manner that the contralateral side which was allocated as an experimental group remains untouched. Further, in these experimental groups (groupI_2, groupII_2 and groupIII_2), different concentrations of *Kalonji* solutions were applied on the gingiva with the help of small cotton pellets soaked in *Kalonji* solution and gingival sulcus on each surface of the tooth was irrigated with 1 ml of solution (16-gauge needle) chosen as per the allotted group. The procedure of *Kalonji* application was repeated for 3 consecutive days. GI and PI were recorded at baseline, 14th day and 28th day of solution application. After the completion of the study, oral hygiene instructions were given to every patient. Results obtained were analyzed statistically.

Statistical analysis

The softwares used for statistical analysis were IBM-SPSS (v21) (IBM, NY, USA) and MS-Excel (Microsoft Corporation, Redmond, Washington). Results were assessed using descriptive statistics and making comparisons among various groups. Discrete (categorical) data were summarized as proportions and percentages (%) and quantitative data as mean ± SD. The statistical evaluation was performed using ANOVA test and Fisher's exact test. $P < 0.001$ was considered as highly significant with $P > 0.05$ as non-significant.

Results

Over all mean age of the patients included in the study in all the three groups, i.e., groups I, II and III was 29.05 ± 6.815 years. According to ANOVA test, no considerable difference ($P = 0.710$) was found among the mean ages of the three groups and therefore, the patients selected were age matched [Table 1]. There was sex predilection of male patients among all the groups with a male-to-female ratio of 3:4 [Table 1].

Gingival index

In inter group comparison of group I (I_1andI_2), no major difference was noticed between the two groups at baseline although a statistically noteworthy difference in GI ($P < 0.001$) was observed between these groups both at 14th day and 28th day with better improvement after SRP in group I_1compared to group I_2 [Table 2].

Similar findings were observed between groups II_1 and II_2 and between groups III_1 and III_2 with comparable GI at baseline and significant difference in GI reduction between groups II_1 and $II_2$and between groups III_1 and III_2 both at 14th and 28th day from baseline [Table 2].

The intragroup comparison through repeated measure ANOVA indicates that SRP-treated groups, i.e., groups I_1, II_1, and

Table 1: Age and sex wise distribution of patients

Group	Age			Sex, *n* (%)		
	Mean±SD	*F*	*P*	Female	Male	*P*
Group I	28.00±6.856	0.349	0.710	4 (57.1)	3 (42.9)	0.854
Group II	28.29±7.994			3 (42.9)	4 (57.1)	
Group III	30.86±6.176			2 (28.6)	5 (71.4)	
Total	29.05±6.815			9 (42.9)	12 (57.1)	

SD: Standard deviation

Figure 1: Group I_1: Patients subjected to scaling and root planing. Group I_2: Patients in which *Kalonji* solution (solution 1) with 1:3 ratio was applied topically on the surface of gingiva and gingival sulcus was irrigated with the same solution

Figure 2: Group II_1: Patients subjected to scaling and root planing. Group II_2: Patients in which *Kalonji* solution (solution 2) with 1:1 ratio was applied topically on the surface of gingiva and gingival sulcus was irrigated with the same solution

Figure 3: Group III_1: Patients subjected to scaling and root planing. Group III_2: Patients in which *Kalonji* solution (solution 3) with 3:1 ratio was applied topically on the surface of gingiva and gingival sulcus was irrigated with the same solution

III_1showed a major mean GI reduction after treatment from baseline to 28th day with F values 502.37, 139.33, and 115.41, respectively (highly significant result). Although on the other hand, the experimental groups treated with solution1 (1:3), solution2 (1:1), and solution 3 (3:1), i.e., groups I_2, II_2 and III_2, respectively, also showed statistically significant reduction in GI from baseline to 28th day but with comparatively lesser reductions in groups I_2 and II_2 (F values 51.25 and 84.95) and higher reductions in group III_2 (F value = 153.75) which was even better than its contralateral control group III_1 (F value 115.41) [Table 2]. Representative figures showing clinical improvements at follow-up periods are shown in Figures 1-3.

Plaque index

On comparing PI among groups I_1 and I_2, no-significant difference in mean PI was observed between them at baseline ($P = 0.436$), but remarkable mean PI reduction was noticed between the groups both at 14th day and 28th day from baseline. In intragroup comparison through repeated measure ANOVA reveals that SRP-treated groupI_1 showed mean PI reduction after treatment from baseline to 14th day with a slight increase after 14th day till 28th day (resultant highly significant PI reduction; F value = 260.06; $P < 0.001$). While solution-treated groupI_2 showed only a consequential mean PI reduction from baseline to 14th day and thereafter till 28thday (resultant insignificant PI reduction; F value = 7.80; $P = 0.007$) [Table 3].

Similarly, between groups $II_1$and II_2 and between groups III_1 and III_2, there was comparable, reduction in PI at baseline, but remarkable mean PI reduction was noticed between the groups both at 14thday and 28thday from baseline. Intragroup comparison through repeated measure ANOVA reveals that in both groups II_1 and III_1, there was a reduction in PI from baseline to 14th days and 28th days (resultant highly significant PI reduction; $P < 0.001$; F value = 419.25 and F value = 575.19, respectively). Whereas, in groups II_2 and III_2 after application of solution 2 (1:1) and solution 3 (3:1), respectively, there was a significant mean PI reduction in group II_2 (F value = 12.48; $P = 0.001$) but highly significant reduction in group III_2 (F value = 30.40; $P < 0.001$) from baseline to 28thday [Table 3].

Discussion

Currently, the concept of "herbalism" for the treatment of various diseases is spreading worldwide owing to its promising results and fewer side effects. As per the World Health Organization, around 60%–80% of the world's population, especially in the developing countries, utilize herbal or traditional remedies for the initial healthcare.[16,17] *N. sativa* (*Kalonji*) is one of the herbs, which has been called as "miracle herb of the century."[18,19]

Several studies have quoted *N. sativa* and its active component TQ showing splendid pharmacological properties for improving human health[18,20,21] However, literature on the use of *N. sativa* for oral care is limited with only a few animal and human based studies highlighting its beneficial role in periodontal diseases.[11,12] Owing to the antibacterial, antioxidant and anti-inflammatory properties of *N. sativa* and its component TQ and its promising results, it was hypothesized that this herb could have a role in preventing the periodontal disease as well.

In the present study, ethanolic extract of seeds of *N. sativa* with glycerine as a carrier was taken in three different ratios, i.e., solution 1 (1:3), solution 2 (1:1) and solution 3 (3:1). A split-mouth protocol was adopted with topical application of solution over inflamed gingiva with subsequent gingival sulcus irrigation without SRP on experimental site and contralateral control side treated with only the gold standard treatment, i.e., SRP in cases of moderate-to-severe gingivitis. The anti-inflammatory effect of different ratios of *N. sativa* solution was assessed as gingival response in the form of change in its color, amount of edema and tendency of bleeding on probing the gingival sulcus by utilizing GI. Further, the antiplaque effect of various ratios of *N. sativa* solution was seen on plaque formation at 14th day and 28th day with the help of PI. Furthermore, the assessment was made as to which ratio of *N. sativa* solution demonstrates maximum anti-inflammatory and antiplaque action. To the best of our knowledge, none of the clinical studies so far have utilized *N. sativa* solution for the management of gingivitis

Table 2: Comparison of gingival index among Groups I_1 and I_2, Groups II_1 and II_2, and Groups III_1 and III_2

GI	Mean±SD		*P*	Mean±SD		*P*	Mean±SD		*P*
	Group I_1	Group I_2		Group II_1	Group II_2		Group III_1	Group III_2	
Baseline	2.16±0.23	2.18±0.39	0.891	2.18±0.41	2.16±0.37	0.604	2.50±0.44	2.59±0.31	0.283
14th day	0.59±0.17	1.88±0.32	<0.001	1.11±0.39	1.73±0.27	0.001	1.23±0.35	1.79±0.39	0.004
28th day	0.16±0.09	1.36±0.24	<0.001	0.29±0.20	0.84±0.16	<0.001	0.27±0.11	0.61±0.20	0.001
Intragroup (*F, P*)	502.37, <0.001	51.25, <0.001		139.33, <0.001	84.95, <0.001		115.41, <0.001	153.75, <0.001	

SD: Standard deviation, GI: Gingival index

Table 3: Comparison of plaque index among Groups I_1 and I_2, Groups II_1 and II_2, and Groups III_1 and III_2

PI	Mean±SD		*P*	Mean±SD		*P*	Mean±SD		*P*
	Group I_1	Group I_2		Group II_1	Group II_2		Group III_1	Group III_2	
Baseline	2.04±0.30	1.96±0.34	0.436	2.07±0.19	2.16±0.21	0.182	2.34±0.20	2.43±0.28	0.054
14th day	0.25±0.10	1.88±0.38	<0.001	0.27±0.09	2.05±0.21	<0.001	0.27±0.13	2.36±0.29	<0.001
28th day	0.30±0.10	1.77±0.34	<0.001	0.20±0.10	2.02±0.25	<0.001	0.16±0.09	2.25±0.25	<0.001
Intragroup (*F, P*)	260.06, <0.001	7.80, 0.007		419.25, <0.001	12.48, 0.001		575.19, <0.001	30.40, <0.001	

SD: Standard deviation, PI: Plaque index

in humans; therefore, a direct comparison with other studies was not possible.

Clinical parameters

All the patients enrolled in groups I, II and III were age matched with a mean age of 29.05 ± 6.185 years and a male-female ratio of 3:4. The mean GI and mean PI for all the groups at baseline showed no statistically significant difference. In intergroup comparison, group I_1showed a statistically highly significant difference in mean GI as compared to group I2 at both 14th and 28th days. It can explain that the main etiological factor for gingivitis is dental plaque which was removed by meticulous scaling procedure in group I_1at baselines resulting in resolution in gingival inflammation with resultant improvement in mean GI. Scaling is a gold standard procedure for the management of gingivitis,[12,22] and therefore, group I_1 patients demonstrated highly significant reduction both in GI and PI at all follow-up time periods.

Patients of group I_2 were treated with topical application of solution 1 with gingival sulcular irrigation without scaling procedure. Although the mean GI showed a significant reduction, it was comparatively less as compared to the scaling groupI_1. Despite the presence of irritating factors in the form of dental plaque which was left undisturbed in group I_2, still the findings are suggestive of reduction in gingival inflammation which might be due to the anti-inflammatory, immune-regulatory, and anti-oxidative properties of TQ, a phytochemical present in *N. sativa*.[11] Supporting to this is a histo-pathological and morphometric study conducted on rat periodontitis that has proven the preventive effects of parenteral TQ in initiation and progression of periodontitis with diminished alveolar bone resorption.[23] There are several studies highlighting the accelerated wound healing of chemically induced oral ulcerinrabbit[24] and chemotherapy-induced oral mucositis in rats[25] by topical *N.sativa*oil. Hence, the anti-inflammatory, immunomodulatory, antibacterial and antioxidant effect with wound healing promoting capacity of its seed extract that was utilized in this study for the formulation of different ratios of solutions could possibly explain for these favorable results.

Further, gingival sulcular irrigation with the solution had an added advantage of antibacterial and anti-inflammatory effects on the inflamed crevicular lining and the remaining periodontal pathogens in the gingival sulcus even after scaling procedure. The efficacy of sub gingival irrigation as an adjunctive procedure has already been shown in number of studies using herbal and chemotherapeutic agents.[26-30]

The mean PI in group I_1 showed a highly significant reduction with comparatively lesser significant plaque reduction in group I_2 from baseline to 28th day. This can be explained that although the original dental plaque was left undisturbed throughout the study, the phytochemicals of *N. sativa* might have shown an antimicrobial effect on dental plaque microorganisms, especially primary colonizers, i.e., *Streptococcus* species,[31] there by preventing its further formation and hence improvement in GI also. Studies emphasizing on its antiplaque effects explain such possibility.[12,31] A study highlighting the antimicrobial role of *N. sativa* on *Aggregatibacter action-mycetemcomitans*, a key periodontal pathogen, emphasizes that this herb could be utilized in oral hygiene products[32] for the treatment of periodontitis as well.

Similar findings were seen between groups I_1 and II_2 and between group III_1 and III_2 with comparable mean GI and PI at baseline. A tall follow-up periods, inter-group comparison between these groups showed a significant difference in both GI and PI at 14th and 28th days from baseline.

In intragroup comparison, the scaling-treated groups, i.e., groups I_1, II_1 and III_1 showed to have a highly significant reduction in both mean GI and PI at the end of the study, whereas solution-treated groups, i.e., groups I_2 and II_2 demonstrated a significant reduction in mean GI with downward trend in mean PI from baseline to 28thday. While group III_2 showed highly significant reduction in both mean PI and mean GI from baseline to 28thday. The overall favorable results in Group III_2 could be owing to the higher concentration of herbal content (3:1) and consequently higher anti-inflammatory and antiplaque action as compared to lower concentration solutions, i.e., solution1 (1:3) and solution 2 (1:1).

Although the literature studies are preliminary and few in number as far as the role of black seed plant (*N. sativa*) in the management of periodontal diseases is concerned,[11-13] the encouraging results from the present study revealed that this herbal plant can potentially be included in dental therapeutics and oral hygiene products.

Conclusion

In the present clinical study, the topical application along with subsequent gingival sulcular irrigation with different solutions of ethanolic extract of *N. sativa,* i.e., 1:3,1:1 and 3:1 in moderate-to-severe gingivitis patients has demonstrated significant reduction in gingivitis index at the end of 28th day from baseline. GroupIII_2 utilizing solution 3 (3:1) provided the better results in the form of highly significant GI and PI reduction. Hence, it is inferred that all three solutions provided improvement in gingival inflammation and deterred plaque formation, but it was not better than the "gold standard," i.e., scaling procedure. However, at the same time, it could have an adjunctive role along with scaling procedure for the management of gingivitis patients.

In addition, *N. sativa* seed extract has shown to have a better wound healing potential, which can be utilized as an adjunct to scaling and root planing (SRP) and during periodontal flap surgery procedures to hasten periodontal wound healing and obtain better clinical soft-tissue healing. The results of the present study are although promising, however, further multi-centric studies with larger sample size at the molecular, cellular and clinical levels are required to investigate the mechanisms of action and clinical efficacy of N. *sativa* and its

constituents, particularly thymoquinone (TQ) to best utilize it for dental advancements.

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Conflicts of interest

There are no conflicts of interest.

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