SYSTEMATIC REVIEW

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Adjunctive therapies in orthodontics: a scoping systematic review



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Abstract

Background Orthodontic tooth movement (OTM) induces physiological and sometimes pathological inflammation in periodontal tissues. This review evaluates the effectiveness of low-level laser therapy (LLLT), vibrational therapy, and probiotics as adjunctive treatments for managing inflammation, pain, and the duration of OTM.

Methods Medline via OVID, Cochrane, EMBASE, and Web of Science databases were utilized to identify randomized controlled trials (RCTs) published between January 1990 and November 2023. Studies were selected based on their evaluation of LLLT, vibrational therapy, and probiotics as adjuncts in fixed orthodontic treatment.

Results LLLT shows promise in enhancing orthodontic tooth movement by accelerating tooth movement and potentially reducing pain. However, disparate study outcomes indicate a need for standardized application protocols. The efficacy of vibrational therapy as an adjunct in OTM remains inconclusive. Some studies in this regard indicate a significant acceleration in OTM but most did not. Probiotic therapy shows potential to improve oral microbiota balance and inflammation but requires more rigorous studies to determine its efficacy and optimal administration methods.

Conclusion Future research should focus on establishing standardized guidelines and protocols to achieve consistent and reliable outcomes across these adjunctive therapies.

Keywords Fixed orthodontic treatment, Low level laser therapy, Orthodontic tooth movement, Probiotics, Vibrational therapy

Introduction

Physiological inflammation in Periodontal tissue during Orthodontic tooth movement

Understanding the effects of orthodontic force on teeth

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is crucial. This force creates compression and tension within the periodontal ligament (PDL), affecting the alveolar bone and its intrinsic constituents, such as blood vessels and nerve endings. This force also leads to changes in occlusion, induces hypoxia (a deficiency in the amount of oxygen reaching the tissues), and promotes vasodilation within the PDL [1].

The mechanical stress caused by orthodontic forces releases inflammatory mediators. These mediators play a crucial role in regulating the activities of osteoclasts (cells that break down bone tissue) and osteoblasts (bone-generating cells), eventually modulating the overall net bone formation, i.e., osteogenesis, thereby contributing to



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bone remodeling [2]. This is a critical process in allowing tooth movement within the jawbone.

In response to orthodontic force, there is an elevated activity of immune factors within the PDL. These include chemokines, growth factors, and cytokines such as interleukin-1 beta (IL- 1 β), interleukin 6 (IL- 6), interleukin 8 (IL- 8), tumor necrosis factor-alpha (TNF α), interferongamma (IFN γ), and prostaglandin E2 (PGE2) [3]. These immune factors actively participate in the inflammatory response and contribute to tissue remodeling.

Tissue-resident Cells of the PDL: The PDL comprises a diverse population of cells with fibroblast-like morphology, including endothelial cells, neuronal cells, epithelial cells, osteoblasts, fibroblasts, and mesenchymal stem/ stromal cells [4]. These collectively contribute to the homeostasis and regenerative processes within the PDL [2, 4].

The interplay between the orthodontic forces, inflammatory mediators, and tissue-resident cells of the PDL results in a dynamic balance of bone resorption and formation, ultimately leading to alveolar bone turnover, leading to alveolar bone turnover [2-4]. This process is crucial for achieving allows controlled tooth movement of teeth to the desired positions during orthodontic interventions (Fig. 1).

Infection-associated periodontal inflammation during tooth remodeling

Infection-associated periodontal inflammation during tooth remodeling is multifactorial. This is particularly the case during fixed orthodontic treatment, with dietary and hygienic habits playing pivotal roles. A cariogenic diet, characterized by a high intake of fermentable carbohydrates, predisposes dental caries development by creating an acidic environment conducive to the proliferation of aciduric and acidogenic bacteria. Concurrently, inadequate oral hygiene due to the appliance itself may foster the development of plaque biofilm of pathogenic microorganisms [5]. These conditions synergize and exacerbate inflammation as the pathogenic bacterial load increases, triggering inflammatory responses in the periodontal tissues (Fig. 2) [6].

Clinical parameters indicative of periodontal inflammation includes a spectrum of notable manifestations.

PERIODONTAL INFLAMMATION FOR TOOTH ALIGNMENT



Fig. 1 Physiological inflammation during tooth remodeling



PATHOLOGICAL INFLAMMATION IN PERIODONTAL TISSUE DURING ORTHODONTIC TOOTH MOVEMENT

Fig. 2 Factors that contribute to pathological inflammation during tooth remodeling (OTM- orthodontic tooth movement)

Bleeding on probing is a premonitory sign of inflammation of the gingival tissues, i.e., gingivitis, followed by periodontitis and increased periodontal pocket depths due to the loss of connective tissue attachment and bone surrounding the tooth. Visibly inflamed gums, characterized by erythema, swelling, and tenderness, are symptomatic of the body's inflammatory response to periodontal pathogens [7]. Additionally, a reduction in alveolar bone level, ascertainable through radiographic examination, signifies the progressive nature of periodontal disease (Fig. 2) [7].

Aseptic periodontal inflammation during orthodontic tooth movement (OTM)

Excessive application of orthodontic forces and duration are identified as non-infectious or aseptic causes of periodontal inflammation [8]. These factors can lead to a pathological retort in the periodontium, the specialized tissue surrounding and supporting the teeth, consisting of the alveolar bone, periodontal ligament, cementum, and gingiva (Figure 2) [8].

Management of inflammation, pain, and duration of tooth remodeling during OTM

Low-Level Laser Therapy (LLLT) In the context of mitigating inflammation and optimizing the timeframe of orthodontic treatment, Low-Level Laser Therapy (LLLT) represents a non-invasive modality that employs low-intensity lasers or light sources to invoke photochemical reactions within cells [9]. These lasers are characterized by their emission of wavelengths in the 800 to 980 nm (nm) range, which supports the development of customized treatment protocols, enabling clinicians to tailor

the laser power output and exposure time to the specific requirements of each treatment [10].

Also, the interaction of laser irradiation with dental tissues is highly selective, with an effective penetration through enamel and dentin. This photobiomodulation is theorized to enhance cellular metabolism, promoting tissue repair and accelerating the ameliorating inflammation within the periodontal tissues affected by orthodon-tic treatment [11].

Vibrational therapy Vibrational therapy is an adjunctive management method that utilizes mechanical vibrations delivered to the dentition and its supporting structures to expedite tissue healing processes. The application of vibrational forces in orthodontics has therefore been evaluated for its potential to enhance bone dynamics that accelerate orthodontic tooth movement [12]. Applying such vibrational forces presumably augments the biological response within the periodontium by modulating the inflammatory response and enhancing tissue remodeling [13, 14]. The process entails stimulating osteoblastic and osteoclastic activities, which are crucial for bone remodeling. Moreover, introducing vibrational force to the periodontal ligament is thought to elevate the basal metabolic rate (BMR) of the alveolar bone, thereby augmenting the cellular activities initiated by orthodontic forces [15]. Commercially available devices such as AcceleDent (OrthoAccel Technologies, Inc., Houston, TX) and Tooth Masseuse have been evaluated for their clinical utility in the application of cyclic vibrational forces directly to the teeth [16].

Furthermore, following orthodontic interventions, patients commonly experience some degree of pain [17], that usually escalates within the first 4 to 24 h after the treatment, and pain subsides thereafter, returning to baseline levels approximately within a week or so [18]. The initial pain is immediate as the applied orthodontic forces compress the periodontal tissues. This temporal pattern of pain intensity reflects the physiological response of the periodontal tissues to the mechanical forces applied during orthodontic procedures [19]. Some studies have also documented that the vibrational forces have mitigated the pain and discomfort associated with orthodontic treatments [18].

Adjunct probiotic use Probiotics as an adjunct during OTM is another emerging therapeutic strategy to control pathological inflammation in the periodontium [20]. Although the inflammatory response is crucial for remodelling the periodontal ligament and alveolar bone so as to facilitate OTM [21], excessive inflammation can lead to periodontal breakdown [21].

In the event probiotics have been shown to balance the oral microbiota, reducing excessive inflammatory responses and permitting the physiological remodelling necessary for tooth movement [20]. The application of probiotics in managing periodontal inflammation during OTM possibly involves a multifaceted mechanism of action that exerts a protective role by inhibition of pathogenic bacteria by competing for adhesion sites on periodontal tissues and dental surfaces [22]. This process is likely to hinder the colonization and proliferation of periodontopathogens, thereby mitigating periodontal inflammation [22].

Select strains of probiotics have been shown to demonstrate antimicrobial properties, such as the secretion of bioactive bacteriocins, hydrogen peroxide, and lactic acid [23]. Moreover, by modulating the host immune response, probiotics interface with the host immune system, potentially downregulating pro-inflammatory cascades [24]. They promote the activity of immunoregulatory cells, which can attenuate the intensity of the inflammatory response, thereby diminishing the risk of tissue damage within the periodontium [21].

Thus, the present review aims to evaluate the evidence supporting the effectiveness of Low-level laser therapy, vibrational therapy, and probiotics as adjuncts in periodontal management during orthodontic tooth remodeling.

Methods

Data sources

A systematic review was conducted using Medline via OVID, Cochrane, and Web of Science databases to identify randomized controlled trials published in English in peer-reviewed journals. The review evaluated the effects of adjunctive therapies, such as low-level laser therapy, vibrational therapy, and probiotic therapy, on patients undergoing fixed orthodontic treatment. The study employed the PICOS framework (Population (P): Patients undergoing fixed orthodontic treatment; Intervention (I): Low-level laser therapy, vibrational therapy, and probiotic therapy as adjunct treatments; Comparison (C): Standard orthodontic treatment without adjunctive therapies or placebo; Outcome (O): Reduction in inflammation and pain, decreased orthodontic treatment duration, and improvements in microbial and periodontal health; Study Design (S): Randomized controlled trials analyzed through a systematic and scoping review approach.

Search terms

The search terms used to select qualifying studies from the database published between January 1990 and November 2023 were as follows:

(periodontal inflammation OR periodontitis) AND (low level laser therapy OR LLLT) AND (orthodontic treatment) AND (randomized controlled trial OR RCT); (periodontal inflammation OR periodontitis) AND (vibrational therapy) AND (orthodontic treatment) AND (randomized controlled trial OR RCT); (periodontal inflammation OR periodontitis) AND (probiotics) AND (orthodontic treatment) AND (randomized controlled trial OR RCT).

(Title/Abstract/Keywords): periodontal inflammation OR periodontitis AND (Title/Abstract/Keywords): LLLT OR low-level laser therapy OR low-level laser AND (Title/Abstract/Keywords): orthodontic treatment AND (Filters): Study Types (Clinical Trials).

(Title/Abstract/Keywords): periodontal inflammation OR periodontitis AND (Title/Abstract/Keywords): vibrational therapy AND (Title/Abstract/Keywords): orthodontic treatment AND (Filters): Study Types (Clinical Trials); (Title/Abstract/Keywords): periodontal inflammation OR periodontitis AND (Title/ Abstract/Keywords): probiotics AND (Title/Abstract/ Keywords): orthodontic treatment AND (Filters): Study Types (Clinical Trials); TS = (periodontal inflammation OR periodontitis) AND TS = (LLLT OR low level laser therapy) AND TS = (orthodontic treatment) AND TS = (randomized controlled trial OR RCT).

TS = (periodontal inflammation OR periodontitis) AND TS = (vibrational therapy) AND TS = (orthodontic treatment) AND TS = (randomized controlled trial OR RCT); TS = (periodontal inflammation OR periodontitis) AND TS = (probiotics) AND TS = (orthodontic treatment) AND TS = (randomized controlled trial OR RCT).

Focused question

What is the effectiveness of adjunctive treatment modalities, employing LLLT, vibrational therapy, and probiotics, in mitigating aseptic periodontal inflammation, treatment duration, and pain reduction in patients undergoing fixed orthodontic treatment?

Primary objective

The study aims to determine adjunctive treatment's efficacy in shortening the treatment duration, fostering tooth movement, and mitigating inflammation and associated pain in patients undergoing fixed orthodontic treatment.

Secondary objectives

To assess the relative efficacy of LLLT, vibrational therapy, and probiotics as adjunctive modalities in mitigating inflammation and pain in patients undergoing fixed orthodontic treatment.

Inclusion criteria

- a. Study design: Randomized Controlled Trials (RCTs)
- b. Randomized Controlled Trials (RCTs) with/out splitmouth design
- c. Setting: Dental settings
- d. Population or country enforced no limitations

Exclusion criteria

- a. Review articles, observational studies, and case reports presenting incomplete outcome details
- b. Studies include patients undergoing other modalities of orthodontic treatment
- c. Studies that do not meet the set study objectives and abstract only
- d. Conference presentations, grey literature

Electronic data search and analysis methodology

This systematic scoping review was structured and articulated following the guidelines set forth by the Preferred Reporting Items for Systematic Reviews and Extension for Scoping Reviews (PRISMA-ScR) [25], ensuring a rigorous and expansive methodological framework. The identification, screening, eligibility assessment, and study inclusion processes are shown in the PRISMA flowchart (Fig. 3), which details the number of sources of evidence screened, assessed for eligibility, included in the review, and excluded based on predefined criteria.

The review was conducted in three phases, starting with an initial screening where four reviewers (KSF, DS, SP, and VHM) independently evaluated the titles and abstracts of articles against the inclusion criteria. The subsequent phase involved a detailed full-text review of the relevant articles, ensuring they met the inclusion standards and aligning their findings with the review's objectives. This stage also included a backward search, reviewing the references of all included articles for additional relevant studies.

The final part of the analysis involved data extraction and quality assessment by two reviewers (KSF, SP, and VHM), with a subsequent verification by another set of reviewers (LPS and VHM) to ensure data integrity.



Fig. 3 PRISMA flow chart of the literature search and study selection

The synthesis of this stage involved mapping out the distinct attributes of each selected study, categorizing them by design, setting, intervention, and scope, followed by a comprehensive evaluation of their findings. All identified references were cataloged using Endnote version 20 (Clarivate Analytics, USA), and the synthesized data from the included studies are summarized in Tables 1, 2, and 3. Meta-analysis was precluded due to the significant heterogeneity among the included studies. Variations in study designs, intervention protocols, outcome measures, and follow-up periods posed challenges in pooling data for quantitative synthesis. Additionally, inconsistent reporting of key data points across studies limited the possibility of meaningful statistical analysis.

Quality and the Overall Risk of bias assessment of studies

In stage three, two reviewers (VHM and KSF) evaluated the methodological quality of the study using the Cochrane Collaboration's risk of bias assessment tool. This involved systematically examining factors such as randomization, allocation concealment, blinding of outcome assessments, selective reporting, and other potential biases. Discrepancies in the evaluation were resolved through discussion until the reviewers reached a consensus, subsequently categorizing the study's bias risk as low, unclear, or high (Table 4).

Results

Effect of adjunct therapies on clinical parameters during teeth alignment

Low-level laser therapy

This review synthesized data from 11 randomized clinical studies [26-36], conducted in several countries, thereby providing an inclusive analysis of the effects of LLLT on fixed orthodontic treatment outcomes, Table 1.

The studies encompassed a diverse demographic of 296 patients of both genders, aged 10 to 40, involving cases and controls ranging from 10 to 94 participants. Orthodontic treatments primarily involve fixed appliances, with some studies using specific configurations such as split-mouth designs, Table 1.

	Clinical Assessment
ooth movement	Type of Laser
ion therapy and orthodontic t	Orthodontic Treatment
Adjunct low-level laser irradiat	No. of patients
Table 1	Study

Study Year Country	No. of patients Age Gender	Orthodontic Treatment	Type of Laser Wavelength Duration of Application Point of application Protocol of Laser irradiation delivery	Clinical Assessment	Outcome
Perignon et al 2021 [26] France	N= 42 Cases = 21 Controls = 21 Age = 10–18 years	Fixed orthodontic treatment	Sirolaser Advance diode laser 970 mm wavelength, 0.5 Watts, and with an energy of 30 J/Cm^2 2 s There are six irradiation points per tooth: 3 buccal and three lingual (cervical, middle, apical third) on canine, premolars, and first molars LLLT application once a month up to 6 months after the first application	Intercanine distance was measured at the time frames M0-M6. M0 is the start of treatment, and M6 is the 6 th month after the first application. The difference between the first month a Class I occlusion was observed, and M0 represents the time it took for a Class I occlusion appearance	Space Closure: Significant acceleration in tooth movement
Zheng et al 2021 [27] China	N= 12 Age: 18–28 years Males =4 Females =8	Fixed orthodontic treatment	Semiconductor diode 810 nm wavelength; 6.29 J/cm2 The 40 s per surface Mesiobuccal, distobuccal, mesio- lingual, and distolingual surfaces of the canine root The procedure was done dur- ing the beginning of retraction and on days 7,14, and 21	The amount of canine retraction was analyzed by scanning the upper arch of each patient on days 0,7,14,21, and 28 Changes observed in the cytokine levels in the GCF in the LLLT group	Space Closure: Tooth movement appeared to be significant upon laser application
Mistry et al 2020 [28] Australia	N= 22 Age = 13-25 years Females: 15 Males: 7	Fixed orthodontic treatment (Split mouth design)	A GaAlAs diode laser a mean wavelength of 808 [SD] 5 nm, power of 0.20 W, and irradi- ance of 1.97 W/cm ² in continuous wave mode 10 s per point The LLLT dose was delivered by applying the laser probe over 8 by applying the laser probe over 8 boints per canine tooth: A. Four points on the buccal side B. Four points on the palatal side A laser regimen was applied on days 0, 28, and 56	The maxillary canine retraction, anchorage loss, and canine rotation were measured digitally A study cast was made every four weeks on days 0, 28, 56, and 84 to assess the amount of tooth movement	Space closure: Applying LLLT every four weeks did not significantly differ in the rate of tooth movement, anchorage loss, and canine rotation during space closure following extraction

Study No. of patients Orthodontic Treatment Type Year Age Vave Year Age Durat Country Gender Nor Country Gender Durat Prott Prott Prott Prott Age Durat Country Gender Low-I DAE N= 38 Fixed orthodontic treatment Low-I 2018 Z91 Age = 40 years Not UAE Not Mentioned 850 n wave, solar UAE Not Mentioned 850 n wave, solar 2018 Z91 Age = 40 years No NA Age 10 conditioned Solar AlSayed H et al N= 94 Fixed orthodontic treatment Active Syria Age = 16-24 years Conti Conti Syria Syria Fixed orthodontic treatment Conti	(pər				
Okla et al N= 38 Fixed orthodontic treatment Low-I 2018 [29] Age = 40 years Not Mentioned with I 2018 [29] Age = 40 years Fixed orthodontic treatment with I 2017 [30] Age = 16-24 years Fixed orthodontic treatment Active Science 2017 [30] Age = 16-24 years Fixed orthodontic treatment Active Science	No. of patients Age Gender	Orthodontic Treatment	Type of Laser Wavelength Duration of Application Point of application Protocol of Laser irradiation delivery	Clinical Assessment	Outcome
AlSayed H et al N = 94 Fixed orthodontic treatment Active 2017 [30] Age = 16–24 years type: type: Syria Age = 16–24 years The la type: The la The la type: type:	N= 38 Age = 40 years Not Mentioned	Fixed orthodontic treatment	Low-level laser therapy (LLLT) with light-emitting diode (LED) delivery 850 nm wavelength, continuous wave, 0.065 J/cm ² 5 min per-arch per day NM	Patients were scheduled every two weeks (\pm 3 days) for intraoral photographs of the maxillary anterior teeth to measure the maxil- lary anterior teeth alignment rate until an irregularity index score of \leq 1 mm was achieved of \leq 1 mm was achieved anterior dentition was assessed on gypsum stone study casts using the irregularity index	De-crowding Maxillary Anterior: Resolution of maxillary anterior crowding was achieved with 35.2% greater efficiency than the controls
Each balve The li to the diculi buccz Each The L The L On 3, days f	N= 94 Age = 16-24 years	Fixed orthodontic treatment	Active Medium: Ga-Al-As Emission type: Continuous Wavelength: 830 nm 1 min/per tooth The laser beam was applied to each root of the six maxillary incisors Each root was divided into two halves: cervical and apical The laser device tip was applied to the center of each half, perpen- dicular to the root and in direct con- tact with the mucosa from both the buccal and palatal sides Each tooth had four application points The LLT application was repeated on 3,7, and 14 days and every 15 days from the second month	The study cast was used for assess- ing outcome measures at four-time points: T0 = before insertion of the first archwire T1 = after one month of treatment commencement T2 = after two months T3 = at the end of the leveling and alignment stage represented by final archwire insertion	De-crowding Maxillary Anterior: Treatment duration and improve- ment in leveling and alignment of maxillary incisor were the sta- tistically significant differences between the two groups The leveling and alignment improve- ment percentage at two-time points were significant T1 = ($P \le 0.004$) T2 = ($P = 0.001$), respectively

Table 1 (contine	ued)				
Study Year Country	No. of patients Age Gender	Orthodontic Treatment	Type of Laser Wavelength Duration of Application Point of application Protocol of Laser irradiation delivery	Clinical Assessment	Outcome
Ureturk et al 2017 [31] Turkey	N= 15 Mean age = 16.2 Males = 7 Females = 8	Fixed orthodontic treatment	gallium-aluminum-arsenide diode 820 nm 10 s per point There are 10 points of application, five on the buccal side and five on the lingual side, distributed as two on the apical portion, two on the cervical portion, and one on the retrical portion, and one on the middle third LLLT was applied on day 0, the 3rd, 7 th, 14 th, 21 st, 30 th, 33rd, 37 th, 44 th, 51 st, 60 th, 63rd, 67 th, 74 th, 81 st, 84 th, 90 th days	3D models were used to analyze canine distalization with the tips of the canines, mesial cusps of the canines, mesial cusps of second molars, and median point of the 3rd palatal raphe as reference points to measure the linear distances. This analysis was carried out on: 10 = before treatment 11 = day 30 12 = day 60 13 = day 90 Changes observed in the cytokine levels in the GCF in the LLLT group	Space Closure LLLT accelerates tooth movement and, therefore, can shorten treatment duration
Dalaie et al 2015 [32] Iran	N= 12 Mean age: ±20.1 (SD) Females: 9 Males: 3	Fixed orthodontic treatment (Split mouth design)	Low-level Ga-Al-As laser (photo lase III, Brazil) Wavelength: 880 nm, 5j/cm ² 10 s LLLT was used at eight spots, once, the dose was given to the canine roots'cervical, middle, and apical priots on buccal and lingual surfaces and at the distopalatal and disto- buccal line angles	The study cast was used to deter- mine the maxillary canine tooth movement after applying force on days 1, 3, 7, 30, 33, 37, 60, 63, and 67	Space closure: There was no significant difference in terms of the rate of tooth move- ment (maxillary canine retraction and pain scores) between the irradi- ated and non-irradiated sides at any time point (P > 0.05)
Genc et al 2013 [33] Turkey	N= 20 Mean age =17.8 Males =6 Females =14	Fixed Orthodontic Treatment	gallium-aluminum-arsenide diode 808 nm wavelength for 10 s 10 points of application, five on the buccal side and five on the lingual side, distributed as two on the apical portion, two on the cervical portion, and one on the middle third LLLT was applied on day 0, the 3rd, 7 th, 14 th, 21 st, and 28 th days after applying the Ni-Ti closed-coil spring	M	Space closure: LLLT accelerated tooth movement significantly

Table 1 (continut	(pa				
Study Year Country	No. of patients Age Gender	Orthodontic Treatment	Type of Laser Wavelength Duration of Application Point of application Protocol of Laser irradiation delivery	Clinical Assessment	Outcome
Doshi-Mehta et al 2012 [34] India	N= 20 Age = 12-23 years Males = 8 Females = 12	Fixed Orthodontic treatment	Semiconductor (aluminum gallium arsenide) diode 810 nm wavelength 10 s On the first day, two irradiations were done on the middle third of the canine's buccal and lingual roots. On days 3,7, and 14, five irradiations were done on the buc- cal side and five on the lingual side of the canine during the first month. The points of application are two doses on the apical third, two doses on the apical third, and one doses on the apical third. This procedure was repeated on day 15 of every month until canine retraction was completed	3 study models were made for each patient. The distance between the first molar and canine was measured at: T0 = day 1 of canine retraction T1: end of 3 months T2: completion of canine retraction	Space closure: An average increase of 30% in the rate of footh movement was observed with the low-intensity laser therapy
Sousa et al 2011 [35] Brazil	W = 10 Mean Age = 13.1 years Males = 4 Females = 6	ΣZ	Diode laser 780 nm 10 s 10 points of application, five on the buccal side and five on the lingual side LLLT was applied on days 0, 3, and 7 LLLT was applied on days 0, 3, and 7	To determine the linear distance between the papilla and canines, the tips of the canines on both sides and the most cervical area in the papilla between the incisors were used as reference points using casts. These measurements were carried out: T1 (when treatment started), T2 (30 days after), T3 (60 days after), T3 (60 days after), T4 (90 days after) Canine retraction measurements were extracted monthly by finding the difference between the linear distances, i.e., T2-T1 and T3-T2	Space Closure: Diode laser accelerated tooth move- ment in orthodontic patients

Table 1 (contin	ued)				
Study Year Country	No. of patients Age Gender	Orthodontic Treatment	Type of Laser Wavelength Duration of Application Point of application Protocol of Laser irradiation delivery	Clinical Assessment	Outcome
Cruz et al 2004 [36] Brazil	N= 11 Ages = 12–18 years	Fixed Orthodontic Treatment	gallium-aluminum-arsenide semi- conductor diode 780 nm 10 s There are 10 points of application, five on the buccal side and five on the lingual side, distributed as two on the apical portion, two on the ervical portion, and one on the middle third LLLT was applied on day 0 and the 3rd, 7 th, 14 th, 30 th, 33rd, 37 th, and 44 th days	A digital electronic caliper was used to measure the dis- tance between the distal slot of the canine bracket and the mesial slot of the first molar bracket on days 0, 3, 7, 14, 21, 30, 33, 37, 44, 51, and 60	Space closure: LLLT accelerates tooth movement sig- nificantly and can shorten the dura- tion of orthodontic treatment
NM Not Mentioned					

Study Year Country	No. of patients Age Gender	Type of Orthodontic treatment	Type of vibration device	Vibration intensity Application protocol and Duration of application	Assessment methods	Reported Outcome
Pérez IA et al 2023 [37] Spain	N = 45 Cases: Group A (N = 14) Group B (N = 15) Control: Group C (N = 16) Age: 21–50 years NR	Orthodontic treatment with clear aligners	AcceleDent Group A: vibrational forces from the onset of treat- ment Group B: vibrational forces at six weeks after treatment onset Group C: No vibration	The vibrational frequency of 30 Hz (Hertz), 0.3 N (Newton) Group A: 20 min/day for six weeks; the aligners were adjusted every seven days for six weeks and then every 14 days until the end of the 18-week study period Group B: 20 min/day for 12 weeks; adjusting aligners every 14 days for the first six weeks, every seven days for the next six weeks, and every 14 days from weeks 12–18	Assessments were done at: Baseline (TO = pre- treatment); 4 weeks (T1); 6 weeks (T2); 12 weeks (T3), and 18 weeks (T4) in all groups except for Group A (T1, T2, except for Group A (T1, T2, movement (bone remodeling): <i>Microbiological Assessment:</i> A paper tip was used to draw crevicular fluid samples from a moving lost RANKL and osteo- protegerin (OPG) levels	Vibrational therapy did not significantly affect bone remodeling in patients undergoing orthodontic treatment with aligners
Mayama A et. al 2022 [38] Japan	<i>N</i> = 48 Cases = 25 Controls = 23 Average age = 20.2 + - 7 years Males = 4 Females = 21	Orthodontic treatment with an edgewise appli- ance	WZ	Vibrations = 5.2 ±0.5 g-forces (gf), 102.2 ±2.6 Hertz 3 min/day at monthly visit	Tooth movement was measured blindly using a 3D model at each monthly visit up to the 8 th treatment visit	Vibrational therapy significantly accelerated tooth movement when sup- plemented adjunct to static orthodontic forces

 Table 2
 Adjunct Vibrational Therapy and Orthodontic Tooth Movement

Table 2 (continued)						
Study Year Country	No. of patients Age Gender	Type of Orthodontic treatment	Type of vibration device	Vibration intensity Application protocol and Duration of application	Assessment methods	Reported Outcome
Telatar et al 2021 [39] Turkey	N = 20 Cases: N = 8 Control: N = 12 Age = 13–18 years Males = 10 Females = 10	Fixed orthodontic treat- ment	AcceleDent	The vibrational frequency of 30 Hertz (Hz) and 0.2 N 20 min/day for six months	Maxillary Canine retraction assessment was con- ducted at the baseline, and the final space closure was distal to the canine lnitial measurements were conducted before the canine tooth was retracted. After was retracted. After measurements were performed again between the mesial edges of the molar tubes and the distal edges of the canine brackets, and the monthly tooth movement rates were recorded as a differ- ence between the initial and after-the-retraction rates. All linear measure- ments were recorded digitally	Vibrational therapy did not have any positive effects on the canine retraction rate
DiBiase et al 2018 [40] UK	N = 81 Cases: Group A (N = 29) Group B (N = 29; sham- identical non-functional device) Control: Group C (N = 27) Age < 20 years NR	Fixed orthodontic treat- ment	AcceleDent	The vibrational frequency of 30 Hz and a force of 0.2 N 20 min/day	Space closure in the man- dibular arch was measured from dental study casts taken at the beginning, subsequent appointment, subsequent appointment, final records were taken after treatment	Supplemental vibratory force during orthodontic treatment with fixed appli- ances does not affect space closure, treatment duration, total number of visits, or final occlusal outcome

Study Year Country	No. of patients Age Gender	Type of Orthodontic treatment	Type of vibration device	Vibration intensity Application protocol and Duration of application	Assessment methods	Reported Outcome
USA USA	N = 26 Cases: Group A: (N = 13) Group B: (N = 13) Age = 18 + years NR	Orthodontic treatment with clear aligners	AcceleDent	The vibrational frequency of 30 Hz and 0.25 N 20 min/day	<i>Clinical Assessment:</i> Digital scans before and immediately after treatment were taken using an iTero intraoral digital scanner (Align Technology) Pain was assessed twice for all subjects dur- ing the study During the initial and middle aligner stages, participants completed the pain survey question- naires, which were to be completed daily for two weeks the treatment irregularity index were compared between the groups	Vibrational therapy did not affect the tooth movement rate (treatment duration) When used with Invisalign, vibrational therapy did not significantly reduce pain related to orthodontic treatment
Pavlin D et al 2015 [42] US	N= 45 Cases: N= 23 Control: N= 22	Fixed orthodontic treat- ment	AcceleDent			Vibrational therapy accelerates tooth move- ment when supplemented with an adjunct to static orthodontic forces
Woodhouse et al 2015 [43] UK	N = 81 Cases: Group A ($N = 29$) Group B ($N = 25$; sham- identical non-functional device) control: Group C ($N = 27$) Mean Age = ± 14.1 Males = 40 Females = 41	Fixed orthodontic treat- ment	AcceleDent	The vibrational frequency of 30 Hz and a force of 0.2 N 20 min/day for 209 ±65 days	Crowding resolution in the mandibular arch was evaluated at the base- line and the final arch alignment. The rate of initial alignment was calcu- alignment was calcu- lated as the difference in the irregularity index of casts taken at baseline and initial alignment divided by the number of days between measure- ments	The supplemental vibra- tional force did not sig- nificantly increase the initial tooth movement rate or reduce the time required to achieve final alignment when used with a pre- adjusted edgewise fixed appliance

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Table 2 (continued)

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Iable 3 Adjul Study Year Country	NCL Problouic Use and P4 Study participants	Medical condition	uon Dental condition Gingival health	Probiotic	Mode of delivery and frequency	Orthodontic treatment	Outcome
Ebrahim et al 2022 [44] Canada	N= 60 Age = 11–18 years NM	Medically fit	No active caries. Mild to moderate plaque accumulation on the teeth Healthy gingiva	The probiotic complex was formulated to con- was formulated to con- including: <i>S. salivarius</i> K12, Five probiotic strains of the genus <i>Lactoba-</i> <i>cillus:</i> <i>Lacticaseibacillus para-</i> <i>casei, Lactiplantibacillus</i> <i>plantarum, Lactoba-</i> <i>cillus salivarius, Ligilactoba-</i> <i>cillus salivarius, Limosilac-</i> <i>tobacillus reuteri</i>	Lozenge Every day for a 28-day	Fixed orthodontic treat- ment lasting six months	There was no sig- nificant change in the PI and composite PI scores in both placebo and pro- biotic groups at each time frame, nor was there a dif- ference in the relative S. <i>mutans</i> count in the saliva and plaque in either of the groups
Alforaidi et al 2021 [45] Sweden	N= 28 Mean Age = 17.3 ± 1.1 years Male = 14 Female = 14	Medically fit	Salivary Streptococcus mutans count was (> 10 ⁴ CFU/ml) NM	Lactobacillus reuteri	Liquid drops containing two <i>Lactobacillus reuteri</i> strains diluted in water Once daily for three weeks	Fixed Orthodontic treat- ment over eight months	A statistically significant increase in plaque pH at three weeks post- intervention was found for the test group ($p <$ 0.05) A statistically insignificant difference in the number of <i>S mutans</i> and lacto- bacill between the two groups ($p > 0.05$)
Benic et al 2019 [46] New Zealand	N= 64 Age range = 10–30 years	WN	Greater than or equal to 20 teeth available NM	Streptococcus salivarius M18	Lozenge Twice daily for 30 days	Fixed orthodontic treat- ment	Oral probiotic <i>S. salivarius</i> M18 reduced the level of halitosis in patients with orthodontic braces but had minimal effects on PI, GI, and dental biofilm microflora
Alp et al 2018 [47] Turkey	N= 45 Age Range = 12-17 years Males = 18 Females = 27	Healthy	Good oral hygiene NM	Kefir group: Lactobacillusand S ther- mophilus Toothpaste group: Bacteriocin	Kefir and Toothpaste Kefir group: 2 × 100 ml daily for six weeks Toothpaste group: twice a day for six weeks	Fixed orthodontic treat- ment	A statistically significant decrease was observed in the salivary <i>S</i> . <i>mutans</i> and <i>Lactobacillus</i> levels in the kefir and toothpaste groups compared with the control group ($P < 0.05$)

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Table 3 (cor	ntinued)						
Study Year Country	Study participants	Medical condition	Dental condition Gingival health	Probiotic	Mode of delivery and frequency	Orthodontic treatment	Outcome
Gizani et al 2016 [48] Grece	N= 85 Mean age = 15.9 Males = 29 Females = 56	No.	Z	Lactobacillus reuteri	Lozenges, Once daily for 17 months	Fixed Orthodontic treat- ment	The patients had generally neglected oral hygiene, both at baseline and at the follow-up There were no differences in the incidence of WSL between the groups at debonding The levels of salivary LB were significantly reduced in both groups ($P \leq 0.05$) at the time of debonding compared with baseline, while no alterations of the MS counts were observed
Pinto et al 2014 [49] Brazil	N= 26 Mean Age = 10–30 years Males = 15 Females = 16	MN	Good oral hygiene No active disease	Bifidobacterium animalis subsp. lactiš DN- 173010	Yogurt The study was divided into four periods. Dur- ing periods 2 and 4, the control and experi- mental groups ate their respective yogurts daily for two weeks. Periods 1 and 3 consisted 0 f a week of a run-in period and four weeks of a wash-out period, respectively	Fixed orthodontic treat- ment	There was no sig- nificant difference between the experimen- tal and control groups (p >0.5)
Cildir et al 2009 [50] Turkey	N= 26 Mean age 12–16 years Males = 8 Females- 18	Healthy	¥Z	Bifidobacterium animalis subsp. lactis DN173010	Yogurt The study was divided into four periods. Dur- ing periods 2 and 4, both groups ate their respective yogurts once daily for two weeks. Periods 1 and 3 consisted of a week of a run-lin period and six weeks of a wash-out period, respectively	Fixed orthodontic treat- ment	Bifidobacterium animalis subsp. lactis DN173010 could reduce salivary streptococci in patients undergoing fixed ortho- dontic treatment

NM Not Mentioned

Table 4 Risk of Bias assessment of the included studies

Studies	Selection bias Baseline characteristics Appropriate control selection	Selection bias Allocation concealment	Selection bias Randomiz- ation	Performance bias Blinding of researchers	Detection bias Blinding of outcome assessors	Reporting bias Selective outcome reporting	Confounding bias
Adjunct low-level laser in	radiation therapy						
Perignon et al 2021 [26]	+	?	+	?	?	+	+
Zheng et al 2021 [27]	+	+	+	?	?	+	+
Mistry et al 2020 [28]	+	+	+	?	?	+	+
Okla et al 2018 [29]	+	?	+	?	?	+	-
AlSayed H et al 2017 [30]	+	?	+	?	?	+	-
Ureturk et al 2017 [31]	+	+	+	?	?	+	-
Dalaie et al 2015 [32]	+	?	+	?	?	+	-
Genc et al 2013 [33]	+	?	+	?	?	+	-
Doshi-Mehta et al 2012 [34]	+	?	+	?	?	+	-
Sousa et al 2011 [35]	+	?	+	?	?	+	-
Cruz et al 2004 [36]	+	+	+	?	?	+	+
Adjunct Vibrational Ther	ару						
Pérez IA et al 2023 [37]	+	?	+	?	?	+	+
Mayama A et. al 2022 [38]	+	+	+	?	+	+	+
Telatar et al 2021 [3 9]	+	?	+	?	?	+	-
DiBiase et al 2018 [40]	+	+	+	?	?	+	-
Katchooiet al 2018 [41]	+	+	+	?	+	+	+
Pavlin D et al 2015 [42]	+	+	+	?	?	+	+
Woodhouse et al 2015 [43]	+	+	+	?	?	+	+
Adjunct Probiotic Use							
Ebrahim et al 2022 [44]	+	?	+	?	?	+	+
Alforaidi et al 2021 [45]	+	?	+	+	?	+	-
Benic et al 2019 [46]	+	?	+	+	?	+	+
Alp et al 2018 [47]	+	?	+	?	?	+	-
Gizani et al 2016 [48]	+	?	+	?	?	+	-
Pinto et al 2014 [49]	+	?	+	+	?	+	-
Cildir et al 2009 [50]	+	?	+	?	?	+	-

Risk Assessment legends: + (Low risk);—(High risk);? (Un-clear risk)

The primary focus is fixed orthodontic treatments, with a detailed examination of low-level laser therapy applications using different Semiconductor Diode Lasers. These lasers operate at wavelengths ranging from 780 to 970 nm, with application durations varying from 2 s to 5 min per point or per tooth, thereby highlighting the significant diversity in laser application protocols, Table 1.

The methodology for laser application varied significantly among the studies. Energy dosage and application frequency for laser irradiation delivery also varied, with some studies applying laser at multiple time points throughout the treatment, ranging from the initial day of retraction up to monthly intervals, to enhance the rate of tooth movement. The points of application included buccal, lingual, cervical, middle, and apical regions of the teeth, particularly focusing on canine roots and maxillary incisors. The clinical assessments typically focused on measures of tooth movement, such as space closure and canine retraction, with evaluations performed at multiple time points throughout the treatment, presented in Table 1.

Clinical assessments were primarily based on digital scans and study casts to evaluate specific outcomes such as maxillary canine retraction and space closure, canine rotation, and the efficiency of de-crowding maxillary anterior teeth. The outcome measures across the studies indicated varying degrees of effectiveness of LLLT in accelerating orthodontic tooth movement, reducing treatment duration, and improving leveling and alignment. Some studies reported significant improvements in tooth movement acceleration [26, 27, 29–31, 33–36], while others found no significant differences when comparing the laser-treated groups and untreated controls [28, 32].

Additionally, some of the reviewed studies [28, 32], employed a split-mouth design to simultaneously compare experimental and control treatments within individual subjects. This method effectively minimizes inter-subject variability and confounding issues.

The collective evidence from these studies suggests that LLLT has the potential to enhance orthodontic treatment outcomes by accelerating tooth movement. However, the degree of effectiveness can vary depending on the parameters such as the laser wavelength, power, and the duration of application, the application protocol, and individual patient responses. This variability underscores the importance of further research to optimize laser application protocols for orthodontic treatments, aiming to achieve more consistent and predictable outcomes.

Vibrational therapy

A total of seven reviewed studies from several countries [37-43] provided a comprehensive overview of the

impact of adjunct vibrational therapy on OTM (Table 2). These studies collectively involved 251 patients, spanning a broad age range from 13 to 50 years, with a balanced representation of genders, via *a vis* the different orthodontic treatment approaches e.g. clear aligners and fixed appliance therapy. The common vibrational device used in these studies was AcceleDent, except for a study conducted in Japan [38], which did not specify the device type used.

These studies reported the application of a consistent vibration intensity of around 30 Hz, with forces ranging from 0.2 N to 0.3 N. The application protocol was relatively consistent, with daily durations of 20 min being the most common, except for a single study by Mayama et al. [38] who used a shorter vibration period of 3 min daily for monthly visits.

These adjunct vibrational interventions were carried out over 6 weeks to 6 months. The workers employed a variety of assessment methods to evaluate the reported outcomes. These included digital scans, clinical and immunological assessments using ELISA kits for RANKL and osteoprotegerin (OPG) levels, and measurements of tooth movement through digital and 3D modeling techniques (Table 2). These methodologies provided an objective measure of the rate of tooth movement and other relevant orthodontic parameters, ensuring the reliability of the findings.

The reported outcomes from these studies were mixed. Most reviewed studies found that vibrational therapy did not significantly affect the rate of tooth movement or pain related to the overall orthodontic treatment process, the canine retraction rate, or the space closure treatment duration. However, Mayama et al. [38] and Pavlin et al. [42] reported that vibrational therapy significantly accelerated tooth movement when used as an adjunct to static orthodontic forces. These cumulative findings suggest that a number of confounding variables, such as the type of orthodontic treatment and the specific protocol parameters, such as vibration intensity and application duration, may influence the impact and effectiveness of vibrational therapy in OTM.

Probiotic therapy

Data from a total of seven randomized clinical trials [44–50], were reviewed to evaluate the effectiveness of adjunct probiotics in fixed orthodontic treatment and to maintain or improve gingival and periodontal health.

The number of enrolled patients in these studies varied, yielding 334 patients. They were predominantly teenagers, ranging in age from 10 to 30. Most participants were reported as medically fit or healthy, with some studies reporting oral hygiene indices, including the plaque index, active caries, and salivary *Streptococcus mutans*

counts. The gingival condition was generally noted as `healthy` in some studies.

The studies employed various probiotic delivery modes, including lozenges, liquid drops, kefir (a fermented milk product), toothpaste, and yogurt. Lozenges were used in multiple studies with daily administration, while liquid drops were diluted in water and taken once daily. Kefir and toothpaste were administered twice daily, and yogurt was consumed daily during specified periods, Table 3. The duration of probiotic administration ranged from a short period of 3 weeks up to a prolonged administration period of 17 months (Table 3).

The reviewed studies illustrate the mixed effectiveness of probiotics in managing oral health during OTM. Some studies reported no significant changes in plaque indices or microbial counts. In contrast, others noted significant improvements in conditions such as salivary pH, reduction in *S. mutans* levels, and decreased incidence of halitosis. For instance, Pinto et al. [49] and Cildir and colleagues [50] used *Bifidobacterium animalis* in yogurt form with contrasting outcomes. While the former [49], reported no significant difference between the control and experimental groups Cildir et al. [50] found a salutary reduction in salivary streptococci. These studies highlight the potential variability in response to the same probiotic strain, possibly influenced by study design or participant characteristics.

In another study, Alforaidi et al. [45] observed a significant increase in plaque pH but no substantial changes in bacterial counts using the strain *Lactobacillus reuteri* as a probiotic. This indicates that the probiotic may have altered the oral ecosystem or the oralome, but not the total population of the microbiota. Ebrahim and others [44] tested multi-strains of probiotics in patients undergoing OTM and did not observe significant changes either in the plaque index or *S. mutans* counts, while Alp et al. [47] reported a decreased level of putatively pathogenic oral bacteria using kefir dietary supplements in combination with a bacteriocin-laced toothpaste.

Gizani and team [48] evaluated the effect of Kefir and probiotic toothpaste groups compared to controls during OTM on the incidence of white spot lesions, a surrogate indicator of caries activity in the oral cavity. They did note a reduction in salivary lactobacillus counts, suggesting a limited impact of the probiotic on enamel demineralization. Benic et al. [46] used another probiotic strain, *Streptococcus salivarius* M18, and reported only a limited reduction in halitosis and minimal impact on other oral health indicators.

Overall, the reviewed studies highlight the variable effectiveness of probiotics in managing oral health during OTM, with some studies showing mildly positive results while others show no significant changes. The variability in outcomes may be influenced by factors such as probiotic strain, delivery mode, study design, and participant characteristics. Clearly, much more research is warranted before any conclusions are made on the beneficial effect of adjunct probiotics daring OTM.

Effect of adjunct therapies on pain during teeth alignment The most common complaint of patients undergoing orthodontic treatment is the overall pain levels, particularly during chewing and biting food [51]. This is likely to be impacted by the age, gender, pain threshold, and the force applied in each individual case.

Some studies have associated LLLT and vibration therapy with significantly reduced pain levels during tooth movement [52, 53]. The mechanism involved in such analgesic effects is unclear, but LLLT is claimed to have antinociceptive and modulating properties [52]. Furthermore, such vibrations induced by LLLT are thought to alleviate PDL compression during tooth movement, thus improving blood supply and preventing the local accumulation of inflammatory mediators. Another potential explanation lies in the 'gate control' theory, which proposes that pain perception may be alleviated through the concurrent stimulation of nerve fibers transmitting nonnoxious stimuli.

However, the RCTs included in the current review did not find significant differences in pain levels between patients in the test and control groups for either LLLT [32] or vibrational therapy. Differences in methods used by multiple investigators and the lack of standardized protocols might explain the mixed results in the literature.

Discussion

Adjunctive use of low-level laser therapy during OTM

Bone remodeling is the most critical physiological process during OTM and involves the dynamic interplay of bone resorption and regeneration around a moving tooth in response to externally applied mechanical forces [54]. Our review data suggest that LLLT has the potential to enhance orthodontic treatment outcomes by accelerating tooth movement. LLLT appears to facilitate such tooth movement via laser-induced biostimulation via multiple molecular and cellular pathways.

Key among these mechanisms is the stimulation of mitochondrial activity, where light absorption by cytochrome c oxidase boosts ATP production. The energy so generated supports cellular functions such as proliferation, differentiation, and migration of osteoblasts and fibroblasts [55]. Additionally, laser-induced biostimulation may enhance the expression of signaling molecules such as RANKL (Receptor Activator of Nuclear factor Kappa-B Ligand) and OPG (Osteoprotegerin). The latter ligand promotes the formation and activity of osteoclasts (bone-resorbing cells), while OPG acts as a receptor for RANKL, inhibiting osteoclastogenesis. Regulating the delicate balance of these molecules is thought to play a crucial role in controlling the rate at which bone is resorbed and formed during tooth movement [56].

several studies we reviewed noted increased retraction velocity on the lased side compared to the control side, most likely due to LLLT-induced biostimulation. Zheng and team [27] and Üretürk et al. [31] noted significant changes in biochemical markers such as IL- 1 β , RANKL, and osteoprotegerin in the gingival crevicular fluid concentrations of the experimental group. The pro-inflammatory cytokine IL- 1 β is secreted in response to mechanical stress and is an early indicator of bone resorption by promoting osteoclast survival, differentiation, and activity [56].

Additionally, significant intra-group and inter-group differences in cytokines, RANKL, and osteoprotegerin markers were also observed in the reviewed clinical trials [27, 31], suggesting a bio-stimulatory effect of LLLT. These results point to synergistic and dynamic bone metabolism through a combination of orthodontic forces and laser treatment. Consequently, LLLT may have potential clinical value in accelerating OTM by eliciting an enhanced biological response in the periodontal tissues subjacent to the teeth where mechanical forces are applied.

The biostimulatory and therapeutic impact of LLLT is proportional to the administered dosage of radiation. Empirical evidence supports that energy densities ranging from 2 to 12 J/cm² are optimal and effectively promote biostimulation, underscoring the importance of precise dosimetric calculations in achieving the desired therapeutic outcomes [53].

Another factor is the wavelength of the laser, which also plays a critical role in determining the biological effects observed. The consensus among researchers is that the optimal range for biostimulation, including in the context of Low-Level Laser Therapy (LLLT), lies within the wavelength range of 550–950 nm. This range appears to maximize the transmission of laser light through the tissue [57].

Interestingly, the employed LLLT wavelength parameters in all the reviewed studies fall within the foregoing range, and this is likely to have led to a significant reduction in the observed duration of treatment. However, several studies [30, 31, 33–36] have failed to provide essential information on the LLLT dosages utilized, which obviates direct comparisons between different studies.

Factors such as the frequency of application of LLLT also play a crucial role in modulating cellular activities

[58]. In our review, the reported disparities in the frequency of applications also presented significant challenges for cross-study comparisons. For instance, Mistry et al. [28], used an 808 nm wavelength laser to accelerate OTM and irradiated the tooth every four weeks for 12 weeks, with no differences observed between the test and the control groups. This could be due to the low frequency of LLLT application, in comparison to others who employed more frequent applications and observed significant differences in the rate of OTM [27, 30, 36]. As diverse LLLT parameters have been shown to expedite OTM to varying degrees, additional research is necessary to ascertain the optimal LLLT dosage, application frequency, and related configurations for maximum therapeutic efficacy.

Finally, in this context, LLLT may also modulate the inflammatory responses elicited by orthodontic forces, possibly mitigating inflammation and pain while enhancing patient comfort [52, 53]. The underlying mechanism for this may be the downregulation of pro-inflammatory cytokine pathways, reduction in leukocyte infiltration, and stimulation of anti-inflammatory mediators [59].

Adjunctive vibrational therapy during OTM

The evidence on the efficacy of vibrational therapy in accelerating OTM is confounding at best, based on our reviews. This may be partly due to the variability in OTM due to factors such as the age, oral hygiene, bone metabolism, and periodontal health of the patient groups [60].

The available data on vibrational therapy in OTM is mainly based on studies using a commercially available, trademarked device called AcceleDent^M. This device operates at a vibration force of 0.25 N and a frequency of 30 Hz [61]. Although a number of investigators have used this device to facilitate OTM only Pavlin and colleagues [42] found it useful for accelerating OTM. Hence, no conclusive evidence can be deduced on the effect of vibrational forces, for accelerating OTM.

There could be several reasons for this apart from the sparsity of the available research on this issue. First, the home usage by patients of a standard device that is not personalized complicates the assessment of its clinical efficacy, as the magnitude of the force applied depends on the position and contact of the mouthpiece (provided by the device manufacturer) and the tooth surface. The mouthpiece does not assure uniform contact across all the teeth across the arch, given the intrinsic variability in the dental anatomy and topography of each individual, such as their tooth height and angulation [62]. Consequently, this could lead to dissimilar force distribution or peak loads across the teeth, resulting in identical devices eliciting varied clinical outcomes, as reported in the reviewed studies. These discrepancies could perhaps be

alleviated to some extent by fabricating personalized tray devices in the future.

Furthermore, the likely idiosyncratic variations in the application patterns of an at-home appliance by different patients could be another factor that contributes to significant differences in OTM due to vibrational therapy. Reviewed studies specifically identified shortcomings in patients' daily application and measurement methods that could have led to unreliable data. For instance, Mayama et al. [38] used a prototype vibration device with a lower vibration force, shorter duration, and fewer applications than AcceleDentTM users and observed a significant outcome in the experimental group.

One possible strategy to overcome such issues and accelerate tooth movement effectively would be to manage the patient under the guidance of an orthodontist during regulated clinic visits. This should lend itself to the delivery of precisely controlled vibrational forces at requisite oral sites. Regular clinic visits allow for close monitoring, adjustment of treatment plans, and timely interventions to optimize the orthodontic treatment process. Animal research findings corroborate such a strategy, demonstrating the benefits of delivering controlled vibrational forces for expedited OTM [63]. Moreover, it is important to regulate the frequency of visits for vibrational therapy, as we noted that some workers employed six-week intervals between orthodontic visits [40], which appeared to be unduly long for assessing any outcomes. either positive or negative.

Hence, the variability in study designs, assessment methods, and outcomes related to orthodontic technologies highlights the need for further research. Additional studies are necessary to define optimal protocols and identify patient populations that may benefit the most from these technologies.

Adjunctive use of probiotics during OTM

The reported variability in outcomes of probiotic use during orthodontic treatment in the reviewed studies suggests that the effectiveness of probiotics may depend on the specific strains of the bacteria used, the delivery methods, and individual patient factors. These findings suggest that while probiotics may alter the composition of the oral microbiota, as is well known, their impact on dental and periodontal health during OTM requires much more research.

Future research directions

The review summary points to the limitations and future research directions regarding three major adjunctive therapies: LLLT, vibrational therapy, and probiotics in OTM.

As for LLLT, future studies should be designed to evaluate the effect of different parameters of LLLT in OTM, mainly because of the contrasting outcomes reported in the currently available data. Laser energy dosage and application frequency may perhaps be more critical than the wavelength of LLLT. Hence, well-designed, appropriately blinded clinical trials with larger sample sizes are needed to establish the optimal dosage and frequency of LLLT exposure for OTM. Finally, uniform treatment guidelines must be promulgated to yield comparable data from different centers [9].

On the other hand, data on the effectiveness of vibrational therapy on OTM is rudimentary at best. The proprietary devices available in the market should be standardized. Larger, age and gender standardised sample sizes are essential as there are differences in growth spurts between males and females during pubertal years. Researcher blinding is essential during participant assignment, while age-related developmental variations should be considered in future such trials.

Finally, future studies on the outcomes of adjunct probiotics during OTM should pay heed to several key factors such as the dosage, specific or strain combinations of bacteria, their administration vehicles, the optimal intervention frequency and dosage duration, and the most suitable delivery method. Additionally, it is essential to evaluate the total microbiome using new tools such as next generation sequencing and MALDI-TOF analyses, during the treatment period. The evaluation of only the specific bacteria is only a quantitative approximation of the salivary microbiota and does not disclose the full microbiome diversity.

Hence, the heterogeneity in protocols for all adjunct therapies limits their direct application in clinical practice. Patient variability and behavioral differences significantly influence outcomes, particularly with adjunct vibrational therapy. Additionally, the sparsity of robust, large-scale probiotics and vibrational therapy trials limits their integration into clinical guidelines.

Conclusion

Low-level laser therapy has demonstrated significant potential in accelerating tooth movement and enhancing patient comfort during orthodontic treatment. However, the limitations highlighted in this review must be addressed in future research to reinforce these findings. Establishing standardized guidelines for laser usage, including specific parameters such as wavelength, power, and duration, is essential for achieving comparable and reliable results. Additionally, the variability observed in the outcomes of vibrational therapy and adjunct probiotic therapy underscores the necessity for further followup studies to bridge the existing gaps and limitations identified in this review.

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Authors' contributions

D.S. contributed to the acquisition, analysis, and interpretation of data. K.S.F. contributed to data acquisition, analysis, interpretation, and manuscript writing. L.S. contributed to the critical revision of the manuscript. V.M. contributed to the critical revision of the manuscript. N.R. contributed to the data interpretation and manuscript writing. S.P. contributed to data interpretation and critical revision of the manuscript. S-G.G. contributed to data interpretation and critical revision of the manuscript.

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Data availability

All data analyzed during this study are included in this manuscript. Further inquiries can be directed to the corresponding author.

Declarations

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