

# INPLASY

## Photobiomodulation effects on biomarkers expression in orthodontic treatment movement: a systematic review

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### ADMINISTRATIVE INFORMATION

**Support** - Data extraction.

**Review Stage at time of this submission** - Data extraction.

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY2024110027

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 November 2024 and was last updated on 7 November 2024.

## INTRODUCTION

**Review question / Objective** The objective of this systematic review is to contrast the existing literature where the expression of molecular biomarkers has been evaluated during orthodontic treatment and the application of PBM, as well as its relationship with the rate of tooth movement, and its participation in reducing the time of orthodontic treatment.

**Rationale** It's common knowledge that absolutely all patients with any type of orthodontic treatment expect to obtain results immediately or as fast as it is possible. Consequently, over the years an attempt has been made to find different possibilities where accelerated orthodontic treatment occurs. Those possibilities are surgical or non-surgical techniques. The surgical techniques have been found to be effective in accelerating the orthodontic movement, nevertheless, they represent an invasive method and could have a significant list of risks and complications to patients. On the other hand, non-

surgical techniques such as mechanical vibrations, chemical techniques, and photobiomodulation (PBM) do not yet provide a sufficient level of evidence to demonstrate they can be used to accelerate orthodontic treatment.

Nonetheless, one of the most promising non-invasive techniques is photobiomodulation therapy, which appears to offer many possible clinical benefits. Furthermore, the mechanisms associated with PBM may be considered as operating at local, regional, and systemic levels. Although the literature mentions that intracellular responses include an increase in activity in mitochondrial metabolism resulting in the elevated production of adenosine triphosphate (ATP), nitric oxide (NO), low levels of reactive oxygen species (ROS) and anabolic effects that stimulate the proliferation and differentiation of osteoblasts, osteoclasts, fibroblasts, and periodontal ligament cells, which triggers bone remodeling, collagen synthesis and revascularization, notwithstanding, it has not yet been fully elucidated how PBM regulates bone metabolism during orthodontic treatment.

**Condition being studied** Photobiomodulation effects on biomarkers expression in orthodontic treatment movement.

## METHODS

**Search strategy** This systematic review adheres to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Statement. According to the PICO guidance, the following research question arises:

What biomarkers have been evaluated and how are they regulated after the application of photobiomodulation in orthodontic treatment and their relationship with the acceleration rate of tooth movement?

The systematic review search strategy was conducted through PubMed, SpringerLink, Cochrane, Scopus, and Web of Science up until March 2024. A manual search in the list of references of the articles used was also performed. The aim of the search was to find studies focused on the biomarkers expressed in orthodontic treatment movement after Photobiomodulation. The main keywords were: “LLL” (low-level laser therapy), “orthodontic treatment” “cells”, “cytokines”, “biomarkers”, “photobiomodulation”, “PBM”, “low-level laser therapy”, “accelerated movement”, “orthodontic tooth movement”, “tooth movement” and “bone remodeling”, in addition to the use of Boolean connectors according to each database.

**Participant or population** Studies of patients who underwent orthodontic treatment plus photobiomodulation in the experimental group and their control group without the application of photobiomodulation.

**Intervention** Application of a photobiomodulation protocol to patients undergoing orthodontic treatment.

**Comparator** Group of patients with orthodontic treatment without the application of photobiomodulation.

**Study designs to be included** RCT’s and CCT’s.

**Eligibility criteria** Inclusion criteria:

- (1) Population: subjects in randomized clinical trials (RCT) and controlled clinical trials (CCT) to whom orthodontic treatment was applied.
- (2) Intervention: photobiomodulation applied during orthodontic treatment.
- (3) Comparison/control: subjects assigned to a control or placebo group to which PBM was not applied during orthodontic treatment.

(4) Outcome: Biomarker expression levels and an indicator of tooth movement rate.

Exclusion criteria:

- (1) Unpublished manuscripts, conference abstracts, and any article that did not have a control group.

**Information sources** PubMed, SpringerLink, Cochrane, Scopus, and Web of Science and a manual search in the list of references of the articles included was also performed.

**Main outcome(s)** Biomarker expression or quantification.

**Additional outcome(s)** Orthodontic tooth movement.

**Data management** Records were imported to the Rayyan QCRI web tool (<https://rayyan.qcri.org>) (14) and it was used for study screening, to read the titles and abstracts, remove duplicate articles, and apply the inclusion and exclusion criteria. Three reviewers (MSCS, LLA, and MACS) working independently screened and evaluated each record and they decided if a study met the inclusion criteria or not. If they disagree with the inclusion of any study in the review, a fourth reviewer (BECS) will decide whether or not to include that study. The reviewers were not blinded to the study title and authorship. Three authors performed the data extraction independently (MSCS, LLA, and MACS) The following items were considered for data extraction: type of study (RCTs and CCTs), sample size, male/woman, groups, age, laser device, wavelength, time spent, orthodontic mechanics, motion measurement, results, and conclusions.

**Quality assessment / Risk of bias analysis** The RCT analysis with the ROB 2.0 tool found that one study was at low risk of bias, two studies were at moderate risk of bias and one study was at high risk of bias. The principal risk factors affecting the methodology of the studies were intended interventions and measurement of the outcomes. The CCT analysis with the ROBINS-I tool concluded that three studies were at low risk of bias, one study was at serious risk of bias and one study was at high risk of bias. The principal risk factor affecting the methodology of the studies was deviations from intended interventions.

**Strategy of data synthesis** The following items were considered for data extraction: type of study (RCTs and CCTs), sample size, male/woman, groups, age, laser device, wavelength, time spent, orthodontic mechanics, motion measurement, biomarker expression, results, and conclusions.

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**Subgroup analysis** The difference in the expression of the biomarkers and the orthodontic movement generated between the experimental group and the control group was considered.

**Sensitivity analysis** All studies where at least the expression of biomarkers was evaluated using photobiomodulation were considered, however, the risk of bias of the included studies was evaluated.

**Language restriction** Only English language articles were included.

**Country(ies) involved** Mexico.

**Keywords** “orthodontic treatment”, “cytokines”, “biomarkers”, “photobiomodulation”, “PBM”, “low-level laser therapy”, “accelerated movement”, “orthodontic tooth movement” and “bone remodeling”.

**Dissemination plans** The results of the work are considered to be published in a journal indexed in JCR with at least one impact factor point. In addition, the work will be disseminated in national and international forums in the area as well as its dissemination to the general population.

#### **Contributions of each author**

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