

# Review Article Role of Medications in Orthodontics: A Review

---

## ABSTRACT

Prescriptions for medications have increased significantly over time. The primary reason for this growth has been the rise in demand for drugs that effectively treat age-related and chronic disorders. Additionally, other variables like health insurance companies and medical ads have had a big impact on the development. Despite the rise in the use of these drugs, researchers claim that children and teenagers are becoming more and more in need of orthodontic treatment. It is evident that individuals who use over-the-counter medications frequently have a variety of consequences from their overuse. Certain pharmaceutical ingredients in these over-the-counter medications may have an impact on remodeling of tissues, the state of tissue homeostasis, and ultimately movement of teeth during orthodontic therapy. In order to concentrate on evaluating and summarizing evidence from previous literatures, as well as examining the effects of regularly used drugs on orthodontic tooth movement, the current review was drafted. Therefore, the goal is to clarify for orthodontists how each drug affects the rate at which teeth shift. This review also discusses some recent pharmacological agents experimented in orthodontics.

*Keywords: Orthodontics, pharmacology, medications, tooth movements*

## 1. INTRODUCTION

The foundation of orthodontic therapy is the idea that exerting stress on a tooth causes mechanical, chemical, and biological reactions to be transmitted to the surrounding tissues. The shifting of the tooth is caused by these structural modifications [1,2]. Bone accretion and resorption refer to the changes that occur in the intervening bone tissue next to the shifting tooth. Resorption of bone is a procedure that occurs when osteoclasts break apart the connective tissue inside bones and liberate minerals into the circulation, whereas the deposition of bones is the procedure by which osteoblasts create fresh bone matrix [3,4].

Whenever mechanical stresses are applied, a biological cascade of events includes remodeling of tissue, cell activation with differentiation, cell strain and extracellular matrix strain with circulation of fluid, which ultimately results in the movement of the tooth [5,6]. Acute seditious reaction, which is defined by pain perception, leukocyte migration out of PDL capillaries, and periodontal vasodilation, is typically linked to the initial phases of tooth movement during orthodontic therapy (TMO). These are the symptoms that most orthodontic patients encounter. However, scientists and orthodontists still do not fully understand the primary conversion mechanism that is enabled by the force produced by the moving tooth [7,8].

But in recent years, scientific developments have made it possible for researchers and orthodontists to investigate the function of certain elements and produced inflammatory mediators, including cyclic adenosine monophosphate (cAMP), collagenase, prostaglandins (PGs) and calcium [9,10]. These mediators play important functions in improving tooth mobility when orthodontic force is applied. The biological sequence of processes described above may provide a succinct overview of current knowledge of intricate connections and processes taking

place alveolar bone and PDL after mechanical stress or chemical mediator activity. These regulators' combined effects with mechanical forces might be inhibitory, preservative, or synergistic [11,12].

Prescriptions for medications have increased significantly over time. The primary reason for this growth has been the rise in demand for drugs that effectively treat age-related and chronic disorders. Additionally, other variables like health insurance companies and medical ads have had a big impact on the development. Despite the rise in the use of these drugs, researchers claim that children and teenagers are becoming more and more in need of orthodontic treatment [13,14]. For example, 7% of kids and teens in the US between the ages of 6 and 17 are taking prescription drugs for behavioral and psychiatric issues. It is evident that individuals who use over-the-counter medications frequently have a variety of consequences from their overuse. Certain pharmaceutical ingredients in these over-the-counter medications may have an impact on remodeling of tissues, the state of tissue homeostasis, and ultimately movement of teeth during orthodontic therapy [15,16].

In order to concentrate on evaluating and summarizing evidence from previous literatures, as well as examining the effects of regularly used drugs on MTO, the current review was drafted. Therefore, the goal is to clarify for orthodontists how each drug affects the rate at which teeth shift. This review also discusses some recent pharmacological agents experimented in orthodontics (Table 1).

## **2. ANALGESICS**

Analgesics are prescription drugs that patients take to reduce pain. It is separated into two categories: non-steroidal anti-inflammatory medications, or "NSAIDs," and non-NSAIDs that don't have anti-inflammatory qualities, like "acetaminophen." The goal of this orthodontic treatment is to reduce pain after applying force to the teeth. NSAIDs are classified into several classes based on their chemical makeup, including salicylates, acrylalkanoic acids (diclofenac), acrylpropionic acids (Profens), oxicams, and coxibs [17-21]. Numerous studies have shown their effects and mechanisms of action by inhibiting the activity of the enzyme cyclooxygenase (COX), which suppresses the synthesis of all prostanoids, including PGs, which are important in the resorption of bones during the orthodontic process and, as a result, lowers the rate of MTO. The effects of a specific COX-2 inhibitor called "Rofecoxib" and a conventional NSAID called "Diclofenac" were examined in relation to the suppression of MTO in rats. The results showed that both drugs significantly impeded dental motion, though partially in the context of Rofecoxib and completely in the scenario of Diclofenac. The impact of celecoxib, an incredibly selective COX-2 blocker, on MTO in rats was documented in a study. They discovered that this type of NSAID prevented tooth mobility and resorption of bone. In an experimental investigation some scientists contrasted the impacts on PGE2 by rofecoxib and acetylsalicylic acid [20-22].

The results of the study indicate that Rofecoxib is a suitable analgesic for controlling pain without impairing the outcome of orthodontic treatment, as acetylsalicylic acid had a stronger inhibitory effect on PGE2 than Rofecoxib did. The same outcome was observed in a new study conducted by Kirschneck et al., 2020 [23], which involved rats. They discovered that because etoricoxib has been shown to have no effect on tooth movement, it is an appropriate analgesic during MTO. Additionally, a number of experiments were carried out to assess how various analgesics affected MTO in both humans and animals. It was discovered that aspirin and ibuprofen use prevent PGE2 synthesis, which modifies tooth movement [24-25]

Conversely, paracetamol was thought to be acceptable to be administered during orthodontic procedures without running the risk of influencing the rate of tooth movement because it had no impact on PGE2 generation. In a similar vein, research has demonstrated that Tenoxicam can successfully manage orthodontic patients' discomfort without affecting the MTO [20-24]. The impact of Prostaglandin E1 (PGE1) injections on moving teeth in humans was assessed in two clinical trials. When contrasted with the control side, they demonstrated a significant advancement in tooth movement on the injected side. Significant variations were noted, including an increase in tooth movement linked to stimulation of the surrounding bones and tissues [21-25]

PGE1 injections at the location of MTO seem to be useful in promoting the alveolar bone's transformation and vascularity. Additional animal studies have demonstrated that local PGE2 treatment quickens MTO [18-24].

## **2. HORMONES MEDICATIONS**

### **2.1 Thyroid Hormones**

The thyroid gland secretes the substances known as thyroid hormones (T3, T4). They are in charge of controlling metabolism. It was discovered that giving thyroxin causes more bone remodeling, which quickens the MTO process [23-25]. As a result, medical professionals should make sure that when prescribing thyroid hormone drugs to orthodontic patients, the dosage is kept low. On the other hand, the thyroid also secretes calcitonin, a hormone that works to lower blood calcium levels in opposition to parathyroid hormone (PTH). By deactivating osteoclasts, it prevents the resorption of bone. Additionally, it increases osteoblasts' capacity to make new bone, which reduces the risk of post-orthodontic relapse, as several animal studies have recently shown [21-24].

Through its impact on the kidney, gut, as well as bone, parathyroid hormone (PTH) is a hormone generated by the parathyroid glands that controls the levels of calcium in the serum. Rats used in animal research have demonstrated that local as well as systemic PTH injections greatly enhanced osteoclast activity and hurried up MTO. These research results clarify that orthodontists should exercise caution while administering PTH medication to patients [24,25].

### **2.2 Oestrogen**

One important sex hormone that controls female bone remodelling is oestrogen. Additionally, it stops a lot of cytokines from being produced, which aids in bone resorption. Furthermore, Oestrogen block the osteoblasts' reaction to PTH. The majority of earlier research assessing the indirect impact of oestrogens on MTO was conducted using experimental methods. Research has demonstrated that oestrogen and calcitonin both slow down the shifting of teeth [24,25] A clinical case report involving a postmenopausal orthodontic patient from among the human research came to the conclusion that MTO might have been delayed by the oestrogens used to treat osteoporosis. Furthermore, female orthodontic patients' teeth moved more quickly during their menstrual cycle than they did during ovulation. Therefore, since oral contraceptives contain oestrogens, which impede tooth movement, orthodontists can take this into account when choosing when to schedule recall visits and whether or not the patient is using any of these medications [21-24].

### **2.3 Relaxin**

Often referred to as a pregnancy hormone, relaxin is an ovarian hormone. It increases the activity of osteoblasts and osteoclasts. Research carried out on rodent subjects suggested that human relaxin could hasten the initial phases of tooth movement in orthodontics and shield orthodontic practitioners against relapse [20-24]. A randomised clinical trial comparing the effects of relaxin and a placebo on the movement and stability of teeth in humans was carried out by a researcher. It was discovered that there were no disparities between groups in shifting of teeth during the course of the 8-week therapy or in relapse 4 weeks after treatment. He ascribed that to the experiment's modest dosage [20-25].

### **2.4 Insulin**

The pancreas produces the hormone insulin, which controls blood sugar levels. Insulin injections are a useful treatment for both forms of diabetes. The consequences of insulin infusion on MTO were documented in two experimental investigations. In the first study, the impact of type 1 diabetes on osteoclast mobilisation and activity was assessed, with an eye towards how this affected the movement of orthodontic teeth in mice [24]. This was contrasted with a different group that received insulin treatment following the induction of diabetes. They discovered that the MTO of the diabetic mice was faster, and that the insulin treatment caused a slower MTO that was comparable to that of normoglycemic rats. A different investigation conducted by another

researcher examined the impact of insulin infusion and hyperglycemia in rats. The findings demonstrated that the bone reaction to orthodontic stresses in individuals with diabetes treated with insulin does not vary much from that of healthy patients [21-25].

## **2.5. Corticosteroids, Immunosuppressive and Immunomodulatory drugs**

Corticosteroids are administered as immunosuppressive and anti-inflammatory drugs. They function by blocking prostaglandin synthesis and calcium absorption in the intestines, which in turn causes a rise in resorption of bone and a direct reduction of osteoblastic activity. The majority of animal investigations found that the chronic group requiring long-term corticosteroid medication had an increase in tooth movement rate [12-24]. On the other hand, investigations on acute corticosteroid consumption revealed decreased bone turnover. According to this research, patients who consume corticosteroids on a regular basis should have their orthodontic force level decreased and maintained more often. Patients who are receiving acute steroid treatment should have their orthodontic treatment delayed until they are off the medication [17-25].

Immunosuppressive and immunomodulatory drugs, which include glucocorticoids, tacrolimus cyclosporine and sirolimus function to reduce the body's capacity to reject an organ transplant. Lupus, psoriasis, and rheumatoid arthritis are a few autoimmune diseases that are frequently treated with other immunosuppressive medications. It has been noted that all of these anti-rejection drugs affect bone mineral homeostasis, which in turn affects MTO. These drugs prevent organ rejection after transplantation [20-24]. Furthermore, the immunosuppressive medication is linked to a number of undesirable side effects, including gingival hypergrowth, which makes maintaining dental hygiene and undergoing orthodontic treatment challenging.

Furthermore, adipocytes, epithelial cells and human immune cells secrete a protein called interleukin antagonists (IL-1RA), which acts as a natural inhibitor of IL1 $\beta$ 's pro-inflammatory effects. The release of these mediators of inflammation on periodontal tissues, which is directly related to bone resorption, characterizes the inflammatory response that occurs after orthodontic loading [21-25]. A study that looked at mice given IL-1RA and found that the mice had less MTO, and osteoclasts corroborated this. The results indicated that IL-1RA likely has anti-inflammatory properties that cause it to downregulate MTO [20-25].

TNF inhibitors are medications that reduce the body's natural reaction to tumor necrosis factor (TNF), a component of the inflammation response. TNF- $\alpha$  antagonists are administered for the management of moderate-to-severe disorders in patients who have failed to respond to traditional systemic therapy, have contraindications, or have developed side effects [21-25]. It was discovered that TNF $\alpha$  is crucial for the recruitment and activation of osteoclasts, either directly or through the production of chemokines. Additionally, a recent study clarified the function of TNF- $\alpha$  in stimulating the generation of sclerostin in osteocytes during MTO on the compression side. TNF- $\alpha$  causes osteocytes to express sclerostin more; subsequently, sclerostin causes osteocytes to express more receptor activator of nuclear factor kappa-B ligand (RANKL). Thus, the study indicated that TNF- $\alpha$  promoted osteoclast development by upregulating sclerostin production in osteocytes during MTO on the compression side [20-22]. Additionally, local injections of integrin inhibitors, such as histatin and RGD peptides, substantially lowered the percentage of lacunae of root resorption and surface areas of root resorption in teeth treated with orthodontics. These injections were also helpful in limiting or preventing MTO of specific teeth in cases where enhancing anchorage was necessary [20-24].

## **3. ANTICANCER DRUGS**

Anticancer medications, also known as antineoplastic medications, are useful in the management of malignant, or cancerous, illnesses. Recent decades have seen a notable rise in the overall incidence of juvenile malignancies. There were no clinical or experimental research on how anticancer medications affected the MTO rate. Nevertheless, it is well recognized that these medications prevent normal cells from proliferating and dividing, which kills cancerous cells as well [24]. As a result, they affect bone remodelling, craniofacial growth, dental development, and growth, which complicates MTO. In a recent study, the durability of orthodontic treatment was evaluated between a group of typically healthy individuals and cancer survivors who had received cytotoxic drug treatment. The authors came to the conclusion that orthodontic intervention

stability amongst cancer survivors is significantly lowered by prior cytotoxic drug therapy, especially in the first year after treatment completion. [25].

#### **4. ANTICONVULSANTS**

A wide class of pharmacological medications used to treat epileptic seizures are called anticonvulsants, or antiepileptic drugs. According to experimental research, carbamazepine and valproic acid are capable of reducing bone density, which may cause rats to develop MTO more quickly [24,25]. However, phenytoin did not have a statistically important impact on the rate of MTO. Gingival expansion that can happen during extended phenytoin usage and make maintaining oral hygiene and orthodontic therapy challenging.

#### **5. BISPHOSPHONATES**

Drugs called bisphosphonates (BPNs) are used for the treatment of osteoporosis and related conditions by preventing the loss of bone density. The systemic as well as local impacts of BPNs on MTO, which reduce resorption of bone, prevent MTO, and postpone orthodontic therapy, have been documented in earlier animal investigations [19-24]. The outcomes from studies regarding orthodontic patients receiving bisphosphonate medication further supported these conclusions. These studies showed that forces applied to the teeth during treatment resulted in longer treatment times, insufficient space closure, impoverished root parallelism, impoverished incisor alignment, and wide PDL with tooth mobility in certain cases. In the event that orthodontic anchoring control is required during orthodontic treatment, these medications would be beneficial [23-25].

#### **6. VITAMIN D**

Along with many other biological benefits, vitamin D is an array of fat-soluble secosteroids that increase intestine absorption of magnesium, calcium, and phosphate. The most significant substance in this class for humans is vitamin D3 (cholecalciferol). According to animal research, localised injections of vitamin D3 accelerated MTO and enhanced the quantity of osteoclasts. Furthermore, identical results were observed in a single randomised clinical trial including patients receiving varying dosages of vitamin D3. It was discovered that clinically and economically, locally administered calcitriol increases MTO in humans in a dose-dependent manner. [12-20].

#### **8. FLUORIDES**

The process of mineralization of the bones and teeth is this medication's primary purpose. Fluoride boosts mineral density and bone mass while also having an impact on tissue metabolism. In a rat experiment, it was discovered that administering sodium fluoride therapy during orthodontic therapy slows the rate of osteoclastic activity and decreases the quantity of active osteoclasts, minimising MTO and thereby extending the orthodontic treatment. However, studies on the impact of fluoride on MTO in humans were conducted to ascertain whether the amount of fluoride in drinking water, whether high or low, had an impact on the early phases of tooth movement when different amounts of orthodontic force were administered. Patients with high fluoride consumption were shown to have greater average rates of shifting of teeth [23-25].

#### **9. FUTURE PERSPECTIVES**

##### **9.1 Topical drug delivery for treatment of oral infections in Orthodontic patients**

When it comes to treating oral infections in individuals receiving orthodontic therapy, topical medicine administration is crucial. In many cases of viral, fungal, and bacterial infections, topical medications have been the first line of treatment for a long time. Topical antimicrobials including antivirals have demonstrated clinical efficacy in numerous clinical trials, offering tailored drug delivery alternatives for the management of localized oral lesions. Topical drug delivery offers several advantages over systemic delivery [25,26]. These include the capacity to deliver drugs more precisely to a targeted site at greater concentrations, a reduced chance of systemic adverse events, the avoidance of drug level variations, inter- and intra-patient variations, and the

ability to be used for self-medication, which improves patient compliance. When applicable, the additional benefits of topical distribution will be discussed. However, there are certain challenges associated with topical medication distribution into the oral cavity, including taste changes, a small surface area, inadequate tissue penetration, and quick elimination because of constant saliva flow, tongue movement, and inadvertent ingesting [24-25].

Typically, topical drug delivery methods have been designed in three different dose forms: liquid (such as sprays and drops), semi-solid (such as gels and ointments), and solid (such as tablets, wafers, films, fibers, and patches). Physiological considerations frequently impact traditional topical dose forms, potentially decreasing the formulation's interaction with the mucosa and resulting in diminished efficacy. Therefore, a variety of approaches have been put out to get around these problems and enhance the way that medications are retained and absorbed in the mouth and throat. Antimicrobials were added to dental cements as well as resins in the 1950s to give localized antimicrobial medication release [20-25].

Treatment techniques for dental disorders have changed as a result of the identification of local antibiotic methods of administration in the control of infections caused by bacteria in the oral cavity. Some of the initial product formulations introduced to the market were minocycline dental gel, metronidazole oral gel, and chlorhexidine chips. Mucoadhesive systems for delivery have been extensively utilized for successful local medication administration in order to prevent the system from being quickly removed from the site where it is applied due to physiological circumstances in the mouth cavity [23-25]. Mucin and mucoadhesive polymer interact to keep the system anchored at the place of application site and to dispense the medication over an extended period of time. Additionally, penetration enhancers are added to delivery systems to produce better systemic and local medication delivery efficacy [25,26].

The disease state must also be considered while developing a local delivery system, since different disease states may call for different medication penetration and retention/distribution patterns in order to achieve optimal efficacy. Most of the time, the medication is needed to reach the underlying layers of epithelium. As a result, different delivery strategies other than standard formulations—such as hydrogels, lipid nanoparticles, polymeric nanoparticle, liposomes, fibers, and films—have been researched for a more effective treatment of infections in the mouth in light of all the conditions listed above. [25,26].

## **9.2 Nanomaterials and polymeric nanoparticles**

In dentistry, materials in the form of drug-incorporated and nano-sized nanoparticles, as well as their combination, have found extensive uses for regeneration of tissue, restorative therapy, and preventive orthodontic treatment usually takes a long time to finish—between one and two years. In order to reduce the length of orthodontic treatment overall, it is imperative to accelerate the rate of tooth movement. Orthodontic relapse, or the tendency for teeth to return to their original locations after orthodontic treatment is finished, is a major problem [23-25]. Since 60% of people worldwide are impacted by this problem, it is critical to put in place efficient procedures to deal with orthodontic relapse. In order to help teeth move and avoid orthodontic relapse, one method in this regard is the targeted application of synthetic and natural medications directly to the area of interest. In addition, scientists are looking at whether it would be possible to use various kinds of nanoparticles to enhance the orthodontic tooth movement process.

Because of their broad-spectrum antibacterial action, metallic nanoparticles including zinc oxide, silver, and gold have been utilized to remove biofilms from the oral cavity. These nanoparticles' wide surface area and elevated charge density allow them to interact more with the negatively charged outermost layer of bacterial cells, which increases their antibacterial action [24-26]. These metals have been coupled with other antimicrobial drugs, such chlorhexidine, to increase their antibacterial action. The combined effect of silver nanoparticles and diode laser group demonstrated the largest decrease in colony-forming units (CFU) when the antibacterial efficacy of gold and silver nanoparticles with diode laser was recently tested against *S. mutans* in teeth sample [24-25].

It has been demonstrated that metallic nanoparticles coated on biomaterial surfaces or mixed with polymers have better antibacterial qualities in the oral cavity. Bismuth subsalicylate nanoparticles have been demonstrated to prevent the growth of multiple periodontal infections,

such as *A. actinomycetemcomitans*, *C. gingivalis*, and *P. gingivalis*, in addition to silver, gold, and zinc oxide [21-25]

Additionally, mesoporous silica nanoparticles—which possess a large surface area and a porous structure—have been studied as anti-biofilm agents. It has been demonstrated that the effectiveness of antibacterial agents against *S. mutans*, *F. nucleatum*, *A. actinomycetemcomitans*, and *P. gingivalis* is increased when coupled with another antibiotic, such as chlorhexidine.

The outstanding mechanical, biological and chemical characteristics of the graphene family of nanomaterials have attracted a lot of interest in dentistry recently. As a graphene derivative, graphene oxide (GO) was studied for its antimicrobial properties against a variety of dental pathogens, such as *S. mutans*, *Fusobacterium nucleatum*, and *P. gingivalis*. It was found that GO nanosheets were very successful in preventing the growth of dental pathogens [25,26].

Transmission electron microscopy was also used to demonstrate how the GO treatment caused the bacteria's cell wall and membrane to break down and allow intracellular substances to seep out. Graphene oxide (GO) is also a promising material for treating oral cavity infections because it has been extensively studied as a nano delivery system for various medications [26].

**Table 1. Recent studies on new pharmacological agents being studied for future perspectives in orthodontic therapy.**

Authors with years	Pharmacological agent investigated	Type of orthodontic therapy investigated	Role in orthodontic therapy
Chang JH et al 2020 [5]	Injectable RANKL,	Accelerated orthodontics	This study demonstrates that injectable preparations incorporating RANKL significantly enhance MTO
Liu X et al, 2022 [7]	Simvastatin encapsulated in exosomes.	Relapse after orthodontic therapy	Simvastatin encapsulated in exosomes increase the inhibitory effect on relapse after orthodontic therapy
Alnajar HAAM, 2021 et al [8]	Calcitonin	Relapse after orthodontic therapy	Systemic doses of calcitonin significantly decrease relapse ration
Murtaza N et al, 2020 [11]	Combined effect of nicotine and caffeine	Orthodontic tooth movement	When nicotine and caffeine are used together, orthodontic tooth movement is increased compared to when they are used separately.
Tian R et al, 2023 [12]	Hederin (Hed)	Alveolar bone resorption	During MTO, Hed may enhance the expression of RANKL and ADRB2 and encourage alveolar bone resorption.

Herniyati H et al, 2023 [13]	Robusta coffee extract ( <i>Coffea canephora</i> )	Expression of FGF2, Collagen-1 and ALP which are bone formation markers. Accelerated orthodontic tooth movement	An alternate substance for quickening orthodontic treatment is robusta coffee extract.
Golshah A et al, 2022 [14]	Caffeine injection	Accelerated tooth movement	Injection of caffeine can significantly increase rate of orthodontic tooth movement
Zhu X et al, 2021 [15]	6-shogaol	Accelerated orthodontic treatment	6-shogaol significantly cause accelerated tooth movement of teeth
Marin GC et al, 2023 [18]	Fluoxetine	Orthodontic tooth movement	The results of this study demonstrate that the quantity of tooth movement is unaffected by long-term administration of 20 mg/kg fluoxetine.
Mehta S et al, 2023 [19]	Alendronate	Orthodontic tooth movement	The rate of MTO was reduced with alendronate.
Gad AM et al, 2023 [20]	Systemic Omega-3 PUFAs	Orthodontic tooth movement	There was substantial proof of the systemic omega-3's osteoclastic inhibitory impact, which decreased the quantity and proportion of MTO.

#### 4. CONCLUSION

The complex chain of events that causes orthodontic tooth movement includes biochemical and mechanical factors, bone cell activity, and modelling and remodeling of the alveolar process in adaptation to mechanical loading. As a result of our growing understanding of how common medications affect the molecules that increase or decrease homeostasis in tissues close to moving teeth exposed to orthodontic forces, orthodontic professionals will need to pay even more attention to their patients' medical and drug consumption histories before and during orthodontic therapy. The current review revealed minimal clinical evidence and mostly experimental evidence for the effects of numerous prescription and over-the-counter drugs on MTO. Certain medications, like acetaminophens, tenoxicam, PGE1, thyroid and PTH, relaxin, long-term corticosteroid consumption, TNF inhibitors, anticonvulsants, and vitamin D3, are MTO promoters. Conversely, a number of medications, including the majority of NSAIDs, calcitonin, oestrogen, insulin, BPNs, acute corticosteroid intake, IL-1RA, and integrin inhibitors, restrict the movement of teeth. As a result, these suppressor medications might work well as an additional orthodontic strategy to improve anchoring and reduce unwanted tooth movement or to stop relapse following MTO.

Furthermore, certain medications such as phenytoin and immunosuppressants may cause unintended orthodontic side effects such gingival hypergrowth, complicating orthodontic treatment and oral hygiene maintenance. Ultimately, it is now evident that additional carefully planned human research is required in order to effectively draw conclusions about how different

drugs affect MTO. Nanomaterials and polymeric nanoparticles and local drug delivery systems for controlling infections in orthodontic patients need to be widely studied.

Orthodontic treatment usually takes a long time to finish—between one and two years. In order to reduce the length of orthodontic treatment overall, it is imperative to accelerate the rate of tooth movement. Orthodontic relapse, or the tendency for teeth to return to their original locations after orthodontic treatment is finished, is a major problem. Since 60% of people worldwide are impacted by this problem, it is critical to put in place efficient procedures to deal with orthodontic relapse. In order to help teeth move and avoid orthodontic relapse, one method in this regard is the targeted application of synthetic and natural medications directly to the area of interest. In addition, scientists are looking at whether it would be possible to use various kinds of nanoparticles to enhance the orthodontic tooth movement process.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## REFERENCES

1. Alam MK, Abutayyem H, Kanwal B, A. L. Shayeb M. Future of Orthodontics—A Systematic Review and Meta-Analysis on the Emerging Trends in This Field. *J. Clin. Med* 2023; 12(2):53
2. Elson A, Anuj A, Barnea-Zohar M, Reuven N. The origins and formation of bone-resorbing osteoclasts. *Bone* 2022; 164: 116538. [<http://dx.doi.org/10.1016/j.bone.2022.116538>] [PMID: 36028118]
3. Muggeo P, Grassi M, D'Ascanio V, *et al.* Bone remodeling markers in children with acute lymphoblastic leukemia after intensive chemotherapy: The screenshot of a biochemical signature. *Cancers* 2023; 15(9): 2554. [<http://dx.doi.org/10.3390/cancers15092554>] [PMID: 37174020]
4. Sennimalai K, Selvaraj M, Mohaideen K, Gothankar G, Arora G. Effect of oral environment on contemporary orthodontic materials and its clinical implications. *J Orthod Sci* 2023; 12(1): 1-8. [[http://dx.doi.org/10.4103/jos.jos\\_73\\_22](http://dx.doi.org/10.4103/jos.jos_73_22)] [PMID: 37351388]
5. Chang JH, Chen PJ, Arul MR, *et al.* Injectable RANKL sustained release formulations to accelerate orthodontic tooth movement. *Eur J Orthod* 2020; 42(3): 317-25. [<http://dx.doi.org/10.1093/ejo/cjz027>] [PMID: 31147678]
6. Omi M, Mishina Y. Role of osteoclasts in oral homeostasis and jawbone diseases. *Oral Sci Int* 2021; 18(1): 14-27. [<http://dx.doi.org/10.1002/osi2.1078>] [PMID: 34220275]
7. Liu X, Muhammed FK, Liu Y. Simvastatin encapsulated in exosomes can enhance its inhibition of relapse after orthodontic tooth movement. *Am J Orthod Dentofacial Orthop* 2022; 162(6): 881-9. [<http://dx.doi.org/10.1016/j.ajodo.2021.07.025>] [PMID: 36117030]
8. Alnajar HAAM, Al Groosh DH. The effects of calcitonin on post-orthodontic relapse in rats. *Clin Exp Dent Res* 2021; 7(3): 293-301. [<http://dx.doi.org/10.1002/cre2.373>] [PMID: 33300289]
9. Alsino HI, Hajeer MY, Burhan AS, Alkhouri I, Darwich K, Alsino HI. The effectiveness of periodontally accelerated osteogenic orthodontics (PAOO) in accelerating tooth movement and supporting alveolar bone thickness during orthodontic treatment: A systematic review. *Cureus* 2022; 14(5): e24985. [<http://dx.doi.org/10.7759/cureus.24985>] [PMID: 35582021]
10. Mheissen S, Khan H, Alsafadi AS, Almuzian M. The effectiveness of surgical adjunctive procedures in the acceleration of orthodontic tooth movement: A systematic review of systematic reviews and meta-analysis. *J Orthod* 2021; 48(2): 156-71. [<http://dx.doi.org/10.1177/1465312520988735>] [PMID: 33546565]

11. Murtaza N, Hamid WU, Shamim A, *et al.* Combined effect of nicotine and caffeine on orthodontic tooth movement in rats. *JIMDC* 2020; 9(2): 109-14.  
[<http://dx.doi.org/10.35787/jimdc.v9i2.462>]
12. Tian R, Xie X, Li J, Du Y, Yin X, Lu X. Effects of hederin (Hed) on alveolar bone microstructure during tooth movement in rats. *J Biomater Tissue Eng* 2023; 13(1): 137-42.  
[<http://dx.doi.org/10.1166/jbt.2023.3236>]
13. Herniyati H, Devi LS, Prameswari N. Analysis of the potency of robusta coffee (*Coffea canephora*) to increase the expression of FGF2, Collagen 1 and ALP in the periodontal ligament during orthodontic tooth movement. *Trends Sci* 2023; 20(8): 6440.  
[<http://dx.doi.org/10.48048/tis.2023.6440>]
14. Golshah A, Omid K, Nikkerdar N, Ghorbani F. Effect of caffeine injection on orthodontic tooth movement in rats: an experimental study on rats. *Int J Dent* 2022; 2022.  
[<http://dx.doi.org/10.1155/2022/7204806>]
15. Zhu X, Yuan H, Ningjuan O, *et al.* 6-Shogaol promotes bone resorption and accelerates orthodontic tooth movement through the JNK-NFATc1 signaling axis. *J Bone Miner Metab* 2021; 39(6): 962-73.  
[<http://dx.doi.org/10.1007/s00774-021-01245-y>] [PMID: 34191125]
16. Ma D, Wang X, Ren X, Bu J, Zheng D, Zhang J. Asperosaponin VI injection enhances orthodontic tooth movement in rats. *Med Sci Monit* 2020; 26: e922372.  
[<http://dx.doi.org/10.12659/MSM.922372>] [PMID: 32323648]
17. Lu W, Li X, Yang Y, *et al.* PTH/PTHrP in controlled release hydrogel enhances orthodontic tooth movement by regulating periodontal bone remodeling. *J Periodontal Res* 2021; 56(5): 885-96.[<http://dx.doi.org/10.1111/jre.12885>] [PMID: 33856055]
18. Marin GC, Johann ACBR, Silva IC, *et al.* The influence of fluoxetine on orthodontic tooth movement in rats. *Braz Oral Res* 2023; 37: e007.  
[<http://dx.doi.org/10.1590/1807-3107bor-2023.vol37.0007>] [PMID: 36700590]
19. Mehta S, Wang K, Chen PJ, *et al.* How does alendronate affect orthodontic tooth movement in osteogenesis imperfecta: An *in vivo* study on a mice model. *Eur J Orthod* 2023; 45(2): 217-23.  
[<http://dx.doi.org/10.1093/ejo/cjad001>] [PMID: 36772933]
20. Gad AM, Soliman SO. Evaluation of systemic Omega-3 PUFAs effect on orthodontic tooth movement in a rabbit model: RCT. *Angle Orthod* 2023; 93(4): 476-81.  
[<http://dx.doi.org/10.2319/110222-750.1>] [PMID: 36928563]
21. Khalaf RM, Almudhi AA. Effects of vitamin D deficiency on the rate of orthodontic tooth movement: An animal study. *Saudi Dent J* 2022; 34(2): 129-35.  
[<http://dx.doi.org/10.1016/j.sdentj.2021.12.008>] [PMID: 35241902]
22. Aoki Y, Kako S, Miyazawa K, *et al.* Dynamics and observations of long-term orthodontic tooth movement and subsequent relapse in C57BL/6 mice. *Exp Anim* 2023; 72(1): 103-11.[<http://dx.doi.org/10.1538/expanim.22-0099>] [PMID: 36261388]
23. Kirschneck C, Wolf F, Cieplik F, *et al.* Impact of NSAID etoricoxib on side effects of orthodontic tooth movement. *Ann Anat* 2020; 232:151585
24. Mitus-Kenig M, Derwich M, Czochrowska E, *et al.* Cancer survivors present significantly lower longterm stability of orthodontic treatment: a prospective case-control study. *Eur J Orthod* 2021; 12.
24. Zahraa Nasser Ahmed, Maha Abdul-Aziz Ahmed, Effects of Common Medications on Orthodontic Tooth Movement: A Systematic Literature Review, *J Res Med Dent Sci*, 2021, 9(7): 149-159
25. Şenel, S., Özdoğan, A.I. & Akca, G. Current status and future of delivery systems for prevention and treatment of infections in the oral cavity. *Drug Deliv. and Transl. Res.* 11, 1703–1734 (2021). <https://doi.org/10.1007/s13346-021-00961-2>
26. Chauhan, Nitasha & Kumar, Mohit & Chaurasia, Simran & Garg, Yogesh & Chopra, Shruti & Bhatia, Amit. (2023). A Comprehensive Review on Drug Therapies and Nanomaterials Used in Orthodontic Treatment. *Current pharmaceutical design.* 29. 10.2174/0113816128276153231117054242.