RESEARCH PAPER

Drugs and Orthodontics: A Comprehensive Narrative Review.

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ABSTRACT

The existing knowledge on pharmacological interactions between commonly used classes of drugs and the outcomes of orthodontic treatment of bones, soft tissues, pain perception, and the immunological environment of the periodontium are critically important determinants of orthodontic tooth movement (OTM) and thus form the subject of the current body of evidence. The pharmacological agents are corticosteroids, bisphosphonates, non-steroidal anti-inflammatory drugs (NSAIDs), calcium channel blockers, antiepileptics, selective serotonin reuptake inhibitors (SSRI), chemotherapeutic agents, hormonal therapies as well as vitamin D and calcium supplementation. Clinical implications such as drug induced gingivial swellings, change in pain thresholds, weak anchorage and managing the medically complex orthodontic patient are also discussed in the review...

Keywords: orthodontic tooth movement; bisphosphonates; NSAIDs; corticosteroids; drug-induced gingival overgrowth; bone remodelling; pharmacology; orthodontics..

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INTRODUCTION

The interface of systemic pharmacotherapy and orthodontics treatment is a clinically relevant, but often undervalued aspect of modern orthodontic practice.2 As the age group of orthodontic patients has expanded, including not only adolescents but a growing number of adults with complex medical histories, there is an increased proportion of patients undergoing systemic pharmacotherapy in orthodontic practice. Biological mechanisms of the orthodontic movement of teeth are inherently based on a complex cascade of cellular and molecular reactions in the periodontal ligament (PDL) and alveolar bone, which are highly susceptible to pharmacological interference.1

The movement of teeth in orthodontics is a result of the sterile inflammation which is caused by mechanical reasons in the PDL. The acts of osteoblasts and osteoclasts are coordinated through the action of applied forces producing tension and compression areas, which activate the release of cytokines, prostaglandins, and neuropeptides.4 This means that any drug that has the potential to alter the rate, predictability, or quality of tooth movement can do so by altering the activity of osteoblasts and osteoclasts, the inflammatory signalling, collagen metabolism, or vascular dynamics.

Regarding the clinical perspective, the implications are extensive. Drugs can slow down or speed up tooth movement, weaken root structure, change soft tissue morphology, have side-effect profiles that can influence patient compliance or pose contraindications to particular orthodontic treatments.2,7 These interactions are thus essential to the safe and effective planning of treatments. The following review is a systematically and evidence-based summary of the key pharmacological interactions that

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pertain to orthodontic practice in the framework of the clinical decision-making models as they are illustrated in the flowcharts that are provided in the appendix (Figure 1).

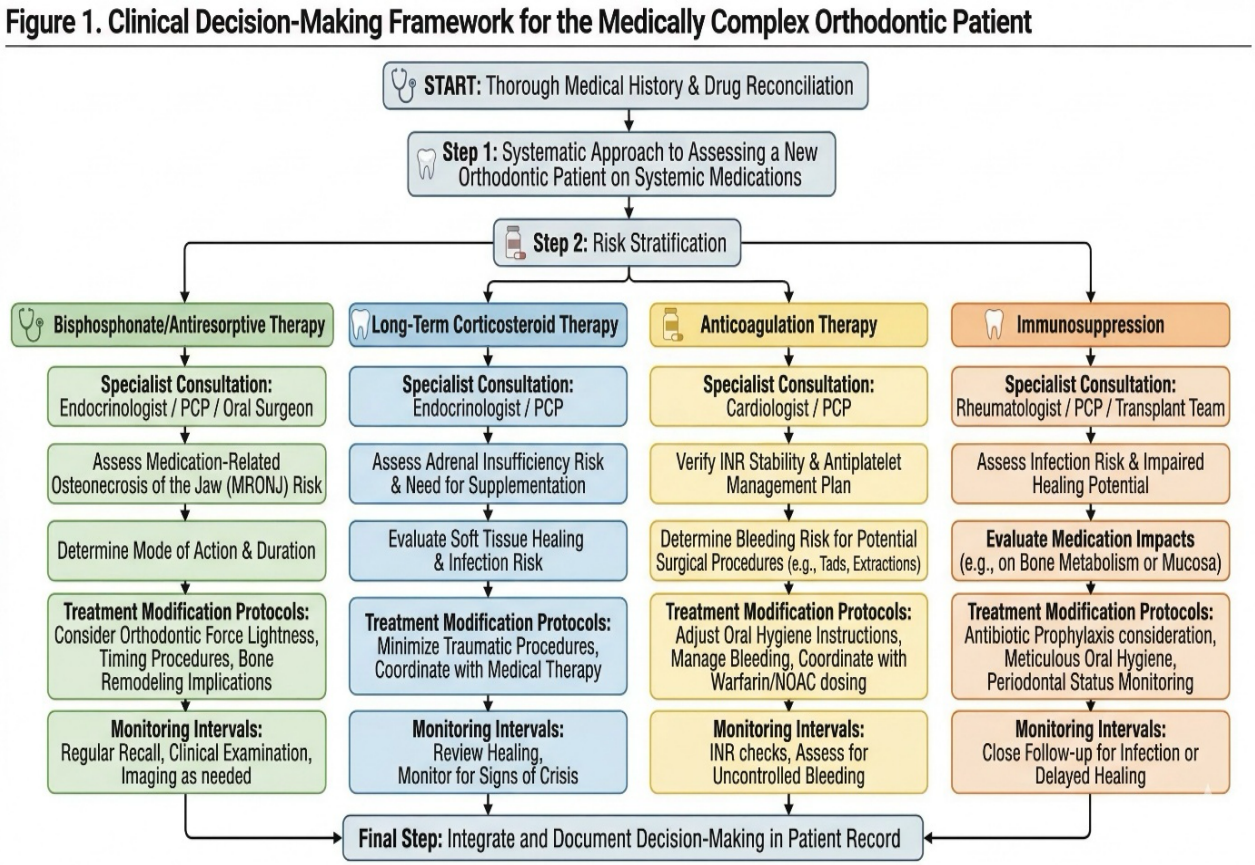

Figure 1. **Clinical Decision-Making Framework for the Medically Complex Orthodontic Patient**

— This flowchart outlines a systematic approach to assessing a new orthodontic patient on systemic medications. Beginning with a thorough medical history and drug reconciliation, the algorithm guides the clinician through risk stratification, specialist consultation pathways, treatment modification protocols, and monitoring intervals. Key branch points include the presence of bisphosphonate use, corticosteroid therapy, anticoagulation, and immunosuppression.

2. Bisphosphonates and Orthodontic Tooth Movement

As an inhibitor of osteoclast-mediated bone remodelling on the pressure side of PDL is a requirement in the occurrence of orthodontic tooth movement,1 BPs provide dose-dependent retardation or near-complete inhibition of tooth movement.7

The studies in animals have consistently shown that systemic and local BP administration decreases the rate of OTM by 4080 percent, depending on the drug, dose and the duration of administration.7 Nitrogen-containing BPs like alendronate, risedronate, and zoledronic acid are stronger than non-nitrogen-containing drugs like etidronate.2 The effects of zoledronic acid on OTM can last long after the drug is stopped despite its prolonged half-life in the skeleton namely over ten years.

The clinical implications are not just retarded tooth movement. BPs can also predispose to orthodontically induced inflammatory root resorption (OIIRR), which may be a result of change in bone quality and alteration of stress distribution within the PDL, perhaps most importantly, orthodontic treatment in high-dose intravenous BP-using patients is in all cases the subject of extremely careful consideration.2

In patients taking oral bisphosphonate therapy to treat osteoporosis, low-dose and long-course regimens, the potential risk of MRONJ is much reduced.6, however, a complete drug history with cumulative duration of therapy and any experience of corticosteroid co-administration (which increases risk) is essential. Risk stratification could be facilitated by liaison with the prescribing physician and, where feasible, serum C-terminal telopeptide (CTX) levels - a system of bone resorption activity - could be measured,2 which is, however, a controversial marker in predicting risk in the literature.6

3. Non-Steroidal Anti-Inflammatory Drugs and Analgesic Agents

NSAIDs represent the analgesic class most commonly encountered in the context of orthodontic pain management. Paradoxically, the prostaglandins that NSAIDs suppress — particularly PGE2 — are among the most important mediators driving osteoclast recruitment and activation on the pressure side of the PDL.[3] Animal studies using systemic indomethacin and ibuprofen have

consistently demonstrated reductions in OTM rate of 20–50%, with the magnitude of effect being dose- and duration-dependent.[7]

The clinical relevance of this interaction in human orthodontic patients remains a subject of ongoing investigation.[7] Short-term, intermittent NSAID use for post-adjustment analgesia — as commonly recommended — is unlikely to produce clinically meaningful interference with long-term tooth movement. However, patients on chronic NSAID therapy for rheumatoid arthritis, ankylosing spondylitis, or other inflammatory conditions represent a different clinical scenario, where cumulative suppression of prostaglandin synthesis may meaningfully retard OTM.[3,7]

Acetaminophen (paracetamol), which does not inhibit peripheral prostaglandin synthesis at therapeutic doses, appears to provide adequate analgesia for orthodontic pain without significantly impeding OTM[3] and is therefore the preferred analgesic recommendation for routine post-adjustment discomfort in patients undergoing active orthodontic treatment. Selective COX-2 inhibitors, while sparing gastrointestinal mucosa, also suppress the prostaglandin pathways relevant to OTM and should be considered equivalent to non-selective NSAIDs in this context.[7]

4. Corticosteroids

Systemic corticosteroids exert complex, pleiotropic effects on the tissues involved in orthodontic tooth movement.[8] On the one hand, corticosteroids suppress the inflammatory cascade that initiates OTM, potentially retarding tooth movement at low or moderate doses.[8] On the other hand, at higher doses and with chronic administration, corticosteroids profoundly impair osteoblast function and reduce bone mineral density, leading to osteoporosis and increased bone fragility — changes that may paradoxically accelerate OTM through reduced resistance to mechanical forces, while simultaneously compromising root and alveolar bone integrity.[7,8]

Patients on long-term systemic corticosteroids for conditions such as asthma, inflammatory bowel disease, rheumatoid arthritis, or following organ transplantation present a constellation of challenges for the orthodontist.[8] These include impaired wound healing, increased susceptibility to periodontal infection, adrenal suppression requiring stress-dosing protocols for surgical procedures, reduced bone density necessitating modified force levels, and drug interactions with other agents in the patient's medication regimen. Supplemental corticosteroid coverage during orthodontic surgical procedures must be considered in patients whose hypothalamic-pituitary-adrenal axis may be suppressed.[8]

Topical and inhaled corticosteroids carry a substantially lower systemic burden and are unlikely to meaningfully affect OTM,[7] though severe oral candidiasis secondary to inhaled steroid use can complicate appliance tolerance and necessitate antifungal management.

Figure 3. Management Algorithm for Drug-Induced Gingival Overgrowth (DIGO) in the Orthodontic Patient

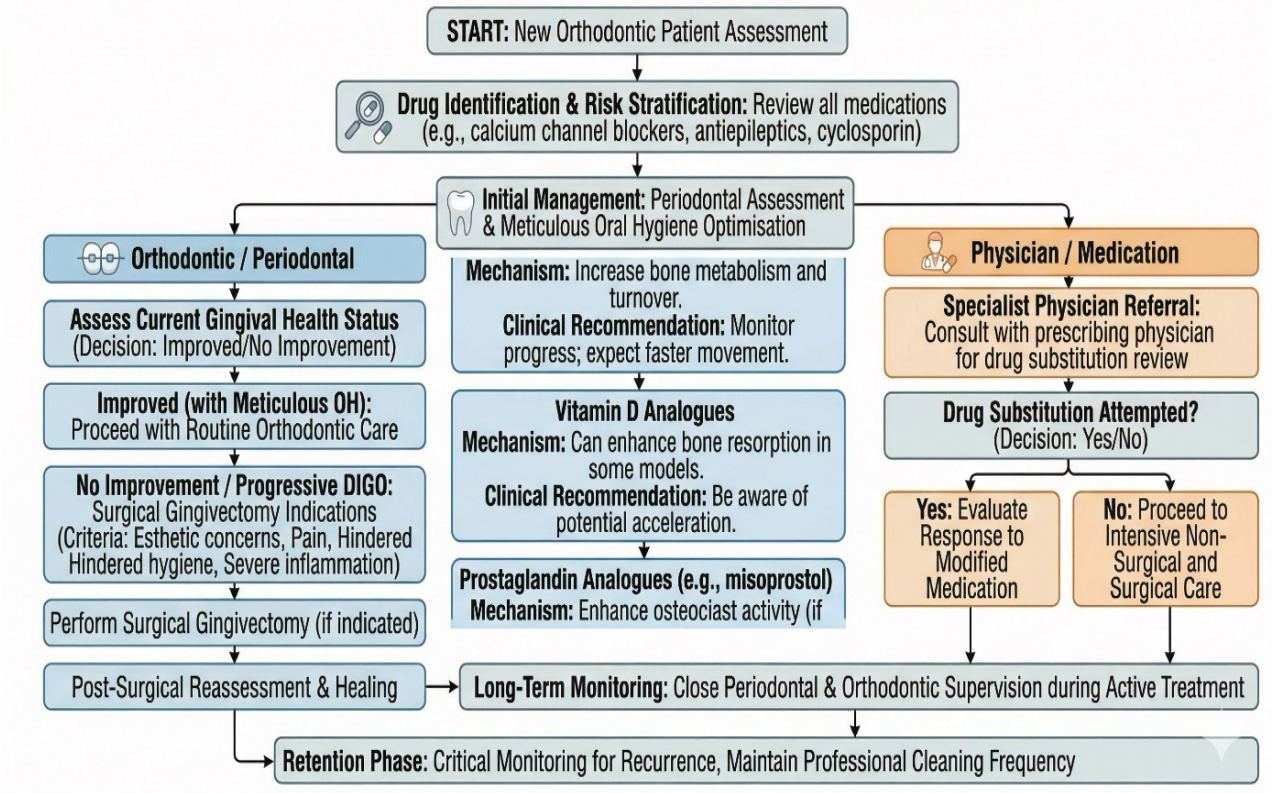

Figure 2. **Effects of Major Drug Classes on the Rate of Orthodontic Tooth Movement**

— *This flowchart categorises pharmacological agents by their net effect on OTM: those that retard tooth movement (bisphosphonates, NSAIDs, corticosteroids), those that may accelerate OTM (thyroid hormones, vitamin D analogues, prostaglandin analogues), and those that alter soft tissue rather than OTM rate per se (calcium channel blockers, antiepileptics, cyclosporin). Clinical management recommendations are indicated at each branch.*

5. Calcium Channel Blockers, Antiepileptics, and Drug-Induced Gingival Overgrowth

Drug-induced gingivial overgrowth (DIGO) is one of the most clinically apparent pharmacological effects that would be experienced in the orthodontic practice; three main classes of drugs are involved; dihydropyridine calcium channel blockers (especially nifedipine and amlodipine), the antiepileptic agent phenytoin, and the calcineurin inhibitor cyclosporin A. The risk of DIGO differs significantly depending on the type of drug and other patient-related predispositions, with incidence ranging between around 15 per cent of amlodipine to above 50 per cent with phenytoin and cyclosporin.5

Pathophysiology The pathophysiology of DIGO has been characterized by the fact that drug-induced changes in the phenotype of gingival fibroblasts result in an augmentation of synthesis and a decrease in degradation of collagen and ground substance in the gingival connective tissue: the same drug will cause much greater overgrowth in the presence of plaque-induced gingivitis in comparison with a healthy periodontal environment.5

DIGO management in the orthodontic patient requires a multidisciplinary approach.5 The basis of prevention and management should be intensive oral hygiene education and plaque care. When it is possible, an attempt at replacement of the offending agent by a pharmacological agent that does not have DIGO risk, e.g. replacing nifedipine with amlodipine with lesser DIGO potential or cyclosporin with tacrolimus, is worth considering in conjunction with the physician of the patient, but the risk of recurrence is high when the offending drug is still used.5

6. Selective Serotonin Reuptake Inhibitors and Psychotropic Drugs.

Skeletal implications of serotonin signalling have become the topic of research interest in the last decade. Serotonin receptors are found in osteoblasts, osteoclasts and osteocytes and gut-derived serotonin has been found to be a strong suppressor of bone formation.10 SSRIs by blocking the serotonin transporter inhibit bone formation, albeit to a modest extent, in epidemiological studies.10

Practically, with regards to orthodontics, patients under antidepressants and anxiogenics may have bruxism and TM dysfunction as a side effect to their drug or mental condition that is predisposed to overlooking orthodontic diagnosis and treatment planning.7, some antipsychotics have the side effect of hyperprolactinaemia; low oestrogen levels, low testosterone levels, and secondary bone loss. Bipolar disorder Lithium has been reported to induce bone growth through Wnt pathway activation, and initial animal evidence indicates that Lithium may enhance OTM - although no clinical study of orthodontic has been done.

7. Hormonal Therapies and Endocrine Influences

The skeletal metabolism has endocrine system-based fundamental control functions, and exogenous hormonal treatments have, accordingly, profound implications in orthodontic treatment.7 Thyroid hormones are highly active bone turnover and bone resorption stimulators. Hyperthyroid patients or patients under supraphysiological thyroid hormone replacement therapy may manifest accelerated OTM, and an increased risk of root resorption.7, hypothyroid patients under inadequate thyroid hormone replacement therapy may show slowed bone remodelling and retarded tooth movement.4

Oestrogen loss, be it menopause, hypothalamic amenorrhoea or premature ovarian insufficiency, results in increased osteoclast activity resulting in accelerated bone loss, and oestrogen replacement therapy (HRT) partially counters this effect. The initial bone quality and its behavior to orthodontic forces is of particular concern in adult women orthodontic patients, especially those in the perimenopausal or postmenopausal phase of life, as anabolic agents like teriparatide (recombinant PTH 1-34), which are increasingly being used to treat patients with severe osteoporosis, have been found in animal studies to dramatically accelerate OTM - an effect with potentially interesting therapeutic possibilities in future studies.

Synthetic oestrogens and progestogens oral contraceptives have not only variable effects on PDL inflammation and bone turnover, which are generally modest at therapeutic doses, but also the interaction of oral contraceptives with tetracycline antibiotics, the latter commonly used to treat acne in adolescent orthodontic patients, is also of clinical interest, tetracyclines potentially decreasing contraceptive efficacy marginally.

8. Targeted Therapies, Immunosuppression and Chemotherapy.

Orthodontist patients involve specific and complicated cases because of patients undergoing or having already undergone oncological treatment. Traditional cytotoxic chemotherapeutic agents have wide antiprolliferative effects, suppressing the function of osteoblasts and osteoclasts, impairing the proliferation of periodontal ligament cells, and potentially causing mucositis, xerostomia, and an increased risk of infection.7 Active orthodontic therapy is usually contraindicated in cases of cytotoxic chemotherapy, and it is important to ensure that treatment is administered in good time with respect to chemotherapy.

Biologic treatments, such as the RANKL inhibitor denosumab and anti-angiogenic agents such as bevacizumab, possess their own distinct risks comparable to or more harmful than bisphosphonates in the context of MRONJ and the bone remodelling impairment.6 Denosumab does not enter bone matrix, and the consequences of such an action are simply speculated about, but, in principle, such an action must be reversible on discontinuation, unlike bisphosphonates.

One of the most difficult orthodontic practice soft-tissue management scenarios is the combination of cyclosporin and nifedipine leading to DIGO,5 an effect that may be

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additive or synergistic, an effect that is mandatory owing to its nephrotoxicity.

Figure 2. Effects of Major Drug Classes on the Rate of Orthodontic Tooth Movement

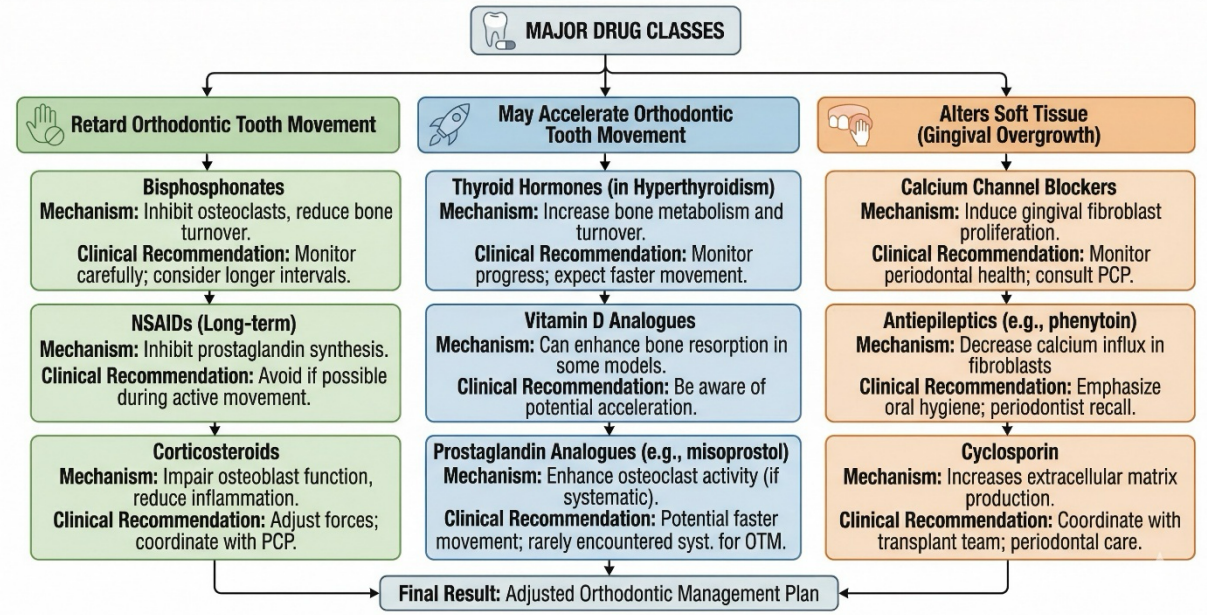

Figure 3. **Management Algorithm for Drug-Induced Gingival Overgrowth (DIGO) in the Orthodontic Patient** — *This decision flowchart presents a stepwise management pathway for orthodontic patients presenting with or at risk of DIGO. The algorithm proceeds from initial drug identification and risk stratification through to oral hygiene optimisation, specialist physician referral for drug substitution review, periodontal reassessment, surgical gingivectomy indications, and long-term monitoring protocols during active orthodontic treatment and the retention phase.*

9. Vitamin D, Calcium, and Nutritional Supplementation

Calcium homeostasis and normal bone mineralisation, which in turn support the quality of the alveolar bone response to orthodontic forces, have been linked to adequate vitamin D status, which is a common issue in most of the world, including South Asian communities. Evidence in animal models that vitamin D supplementation may speed up OTM, possibly by changing RANKL/OPG ratios and increasing osteoclast activity,7 is not clear regarding the clinical relevance of this effect in patients with orthodontics with corrected deficiency.

Pharmacological doses of vitamin D analogues (e.g., calcitriol) as opposed to nutritional supplementation doses are more likely to have an effect on bone turnover and OTM.7 Calcium supplementation per se is not likely to have a direct pharmacological effect on OTM but may have an effect on bone density in the presence of either deficiency states or osteoporosis induced by corticosteroids.8

10. Clinical Recommendations and Conclusions.

Pharmacological environment of the modern orthodontic patient requires a planned, proactive approach to drug-associated risk evaluation and modification of the treatment.2,7 A complete history of medication, such as prescription medications, over-the-counter medications, hormonal medications, and nutrition supplements, must be gathered and updated with each clinical check-up. The orthodontist should also have adequate pharmacological literacy to identify drugs with clinically important skeletal, soft-tissue or immunological effects, and solicit relevant specialist advice where necessary.7

The main, practical, recommendations that arise as a result of this review are as follows: first, patients on a bisphosphonate regimen should be counselled about the occurrence of slower tooth movement and about risks associated with invasive treatment; MRONJ risk stratification will need to be conducted in conjunction with the prescribing physician; second, fixed appliance-therapy in patients on immunosuppressive therapy necessitates increased periodontal monitoring and may require surgery intervention; third, close collaboration with their medical team is needed in orthodontic treatment of patients, who are on imm

The new pharmacological strategies such as the use of prostaglandin analogues on local basis, low level laser therapy to alter the inflammatory environment and experimental use of RANKL-targeted therapy to alter OTM form a new frontier in the pharmacological information on orthodontics and the clinical imperative to negotiate the interactions between therapeutic agents and the biological processes of orthodontic therapy.

To sum up, the interaction between drugs and orthodontics occur at many levels, at the molecular, cellular, tissue and systemic level, the consequences of which are both clinically insignificant and profoundly limiting to the treatment of an ever more medically complicated patient base.1,7 The reason is that a comprehensive understanding of the interaction between drugs and orthodontics is no longer a pleasant addition to the orthodontic knowledge

base, but an indispensable competency of the modern clinician in practice..

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