



“Bisphosphonate 2.0”: Recent Advancements and Future Perspectives in Dentistry- A Narrative Review.

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ABSTRACT :

Bisphosphonates are potent antiresorptive drugs primarily used to treat osteoporosis and to manage cancers. Because they bind well to bone and reduce osteoclast activity, they have become more important in dentistry. Recent studies now look beyond the risk of medication-related osteonecrosis of the jaw (MRONJ) and explore their use in treating gum disease, supporting dental implants, preserving jawbone, treating jaw conditions, and improving implant surfaces. Current evidence shows that using these drugs for osteoporosis does not, seem to raise the risk of dental implant failure, but long-term use may slightly increase the risk of MRONJ. Promising areas include delivering bisphosphonates directly to the mouth and using them on implant surfaces, though a 2026 review found insufficient evidence of clear clinical benefits. New research is focusing on targeted drug delivery, advanced implant coatings, managing the bone-immune environment, personalizing MRONJ risk, and more precise treatments. This review covers the latest developments and future possibilities for bisphosphonates in gum treatment, dental implants, oral surgery, and prosthodontics.

Keywords: Bisphosphonates; Antiresorptive drugs; Dentistry; MRONJ; Dental Implants; Implant surface modification; Bone remodeling.

Introduction

Bisphosphonates have had a complicated role in dentistry. They can help protect the bone around teeth and implants by slowing bone loss, but if they suppress bone remodeling too much, they can cause medication-related osteonecrosis of the jaw (MRONJ), especially in patients at higher risk.

Because of these mixed effects, researchers are looking for ways to use bisphosphonates more carefully and locally, rather than giving them as a whole-body treatment. Recent literature has expanded the potential dental applications of bisphosphonates to: [1]

- Periodontal bone preservation
- Peri-implant bone maintenance
- Implant surface functionalization
- Localized drug delivery
- Treatment of selected jaw disorders
- Modulation of orthodontic tooth movement
- Bone-regenerative strategies.

A 2025 review described the dual effects of bisphosphonates on bone metabolism and implant osseointegration, and highlighted the need for optimized systemic/local drug delivery, novel coatings, and individualized implant strategies.

From Systemic Antiresorptive Drug to Dental Biomodulator

The traditional concept is:

Systemic bisphosphonate → osteoclast inhibition → reduced bone resorption

The emerging concept is: Targeted/local bisphosphonate → controlled osteoclast modulation → preservation of peri-implant/alveolar bone. This represents an important conceptual shift.

Instead of asking: “Should bisphosphonates be avoided in dentistry?”

research is increasingly asking: “Can the antiresorptive properties of bisphosphonates be precisely controlled and harnessed for dental applications?” [2]

Recent Advancement [3-5]

1. Bisphosphonates as Adjuncts in Periodontal Therapy

Periodontitis is characterized by inflammation-associated destruction of periodontal supporting tissues and alveolar bone. Because osteoclast activation is an important component of periodontal bone destruction, bisphosphonates have been investigated as adjunctive agents.

Proposed mechanism: Periodontal inflammation ----Pro-inflammatory cytokines ----Osteoclast activation ----Alveolar bone resorption ----Bisphosphonate ----Osteoclast inhibition ----Reduced bone resorption ----Potential preservation of alveolar bone.

Recent evidence: A 2025 review examined 15 studies involving 776 postmenopausal women with gum disease who were treated with bisphosphonates. The studies tested the effects of zoledronic acid, alendronate, and risedronate, administered in different ways, including by mouth, by injection, and directly to the gums. Many studies have found improvements in gum health, but the authors said more rigorous studies are needed to identify the best treatment methods and ensure they are safe in the long term.

Future direction

The best approach may not be long-term whole-body treatment, but rather: Local periodontal delivery → high concentration at diseased site → reduced systemic exposure → targeted osteoclast modulation.

Potential delivery systems include: Local gels, Microspheres, Nanoparticles, Injectable hydrogels, Periodontal chips and Biodegradable carriers.

2. Bisphosphonate-Modified Dental Implant Surfaces

A major new development is the creation of dental implants with bisphosphonates built into their surfaces. Instead of administering bisphosphonates systemically, the drug can be attached directly to the surface of a dental implant.

Concept

Implant surface ----Bisphosphonate immobilization/loading ----Localized antiresorptive activity ----Reduced osteoclast-mediated bone resorption ----Potential preservation of marginal bone. This approach attempts to obtain the desired local biological effect while minimizing systemic exposure.

Nanotechnology and Surface Engineering

Future implant surfaces may combine bisphosphonates with Nanostructured titanium, calcium phosphate, bioactive glass, polymer coatings, antibacterial nanoparticles, and Growth factors. This means future implants could help bone attach, fight osseointegration, and bone loss, instead of just being a simple titanium post.

Does Bisphosphonate Actually Improve Implant Success?

Recent evidence is important here. A 2026 review examined the use of bisphosphonates locally and on implant surfaces. Some studies have shown promising biological effects, but overall there is not yet enough evidence that they improve implant-bone bonding or prevent bone loss. The authors said more high-quality evidence is needed to provide conclusive evidence.

So, bisphosphonate-coated implants should not yet be considered a standard treatment.

Current status:

Biologically promising → clinically investigational.

3. Reconsidering Bisphosphonates and Dental Implants

Another important recent development is the reassessment of whether systemic bisphosphonate therapy should automatically preclude implant treatment. A 2025 International ONJ Taskforce systematic review and consensus statement found that, in patients with osteoporosis, antiresorptive therapy does not need to be routinely stopped before implant placement. The evidence did not demonstrate an association between antiresorptive therapy and implant failure, although long-term bisphosphonate use may be associated with a small increase in MRONJ risk. This marks a big change from previous strict rules. This means that using bisphosphonates for osteoporosis does not automatically rule out dental implants. However, this does not apply to patients who are on high doses of these drugs for cancer.

4. Evidence-Based Implant Risk Stratification

Rather than categorizing patients simply as: “Bisphosphonate user” vs “non-user,” contemporary approaches emphasize individualized risk assessment. Important variables include:

Drug-related: Potency, Route, Dose, Duration and Cumulative exposure.

Patient-related: Osteoporosis vs malignancy, Diabetes, Smoking, Corticosteroid use, Cancer therapy and Previous MRONJ.

Oral factors: Periodontitis, Periapical infection, Peri-implantitis, Oral hygiene and Prosthetic trauma.

Procedure-related: Extraction, Implant placement, Bone augmentation and Extensive periodontal surgery. This approach is increasingly referred to as a personalized MRONJ risk assessment.

5. Bisphosphonates and Peri-Implant Bone Preservation

The biological rationale is particularly interesting. After implant placement, bone undergoes continuous remodeling.

Excessive osteoclast activity may contribute to:

Marginal bone loss → peri-implant instability → implant complications

Bisphosphonate-mediated suppression of osteoclasts could theoretically reduce this process.

However, excessive suppression creates the opposite problem:

Reduced remodeling → impaired adaptation/healing → potential MRONJ

Future research needs to strike the right balance between insufficient and excessive antiresorptive activity. Recent studies indicate that the amount of the drug, when it is given, and how it is delivered are all important factors in improving outcomes.

6. Bisphosphonates in Rare Jaw Disorders

An emerging area involves the use of antiresorptive therapy in selected rare bone disorders. A new area of research involves using antiresorptive drugs to treat rare jawbone diseases, such as central giant cell granuloma, aneurysmal bone cyst, and diffuse sclerosing osteomyelitis. The evidence is still early, and these uses are not yet standard treatments. A 2025 review found these drugs promising for some rare jaw conditions, but more research is needed to establish treatment guidelines and confirm safety.

The direction is the relationship between:

osteoclasts + immune cells + inflammatory mediators + bone remodeling.

The traditional model considered osteoclasts primarily as bone-resorbing cells. The emerging concept of osteoimmunology recognizes that osteoclasts are closely linked with T cells, B cells, macrophages, cytokines and inflammatory mediators.

Future bisphosphonate strategies may therefore attempt to regulate the bone-immune microenvironment. Future strategies with bisphosphonates may focus on managing the bone-immune environment rather than simply stopping osteoclasts everywhere. Recent reviews highlight this as an important area for future research. Systemic bisphosphonate therapy to Site-specific bisphosphonate delivery.

Potential systems include:

Nanoparticles → targeted delivery

Hydrogels → sustained release

Microspheres → controlled local concentration

Implant coatings → direct bone-implant interface delivery

Periodontal delivery systems → localized treatment of periodontal defects.

The goal is: Maximum local biological effect with minimum systemic exposure.

7. Bone-Immune Microenvironment

A particularly interesting future direction is the relationship between:

Osteoclasts together with immune cells and inflammatory mediators are involved in bone remodeling. The conventional view was that osteoclasts were primarily cells that resorb bone; the new idea in osteoimmunology, however, holds that osteoclasts are closely associated with T cells, B cells, macrophages, cytokines, and inflammatory mediators.

Future bisphosphonate strategies may therefore aim to regulate the bone-immune microenvironment rather than simply suppress osteoclasts globally. Recent reviews specifically identify modulation of the bone immune microenvironment as an important future research direction.

8. Localized Drug Delivery

In the future, we may see a shift from:

systemic bisphosphonate therapy to site-specific bisphosphonate delivery. Some possible systems include nanoparticles for targeted delivery, hydrogels for sustained release, microspheres for controlled local concentration, implant coatings for direct delivery at the bone-implant interface, and periodontal delivery systems for localized treatment of periodontal defects. The aim is to achieve the greatest local biological effect while keeping systemic exposure as low as possible.

9. Combination Therapies

In the future, implant surfaces might include bisphosphonates along with other biologically active molecules.

For example, bisphosphonates could be combined with BMP-2. One possible idea is that BMP-2 could help stimulate bone growth. Bisphosphonates may inhibit osteoclasts, which could help create a better balance between bone formation and resorption.

Researchers are also looking into other combinations, such as bisphosphonates with hydroxyapatite, calcium phosphate, antimicrobial agents, growth factors, or stem-cell-based methods. These approaches are still experimental and need thorough safety testing.

10. Digital and Personalized Risk Prediction

Future prevention of medication-related osteonecrosis of the jaw (MRONJ) may incorporate bone conduction therapy (BCT), digital intraoral scanning, artificial intelligence, electronic medication records, patient risk factors, bone density measurements, and treatment history.

An artificial intelligence-assisted model could estimate an individual patient's risk prior to intervention. Such interventions include tooth extraction, dental implant placement, bone grafting, and periodontal surgery. The ultimate objective is to develop a personalized MRONJ risk score. However, clinically validated predictive models are required before these approaches can be routinely implemented.

Future Perspective [6,7]

A. The Therapeutic Window

One of the most important future concepts is identifying an optimal therapeutic window for bisphosphonates.

Too little antiresorptive activity: → excessive bone resorption.

Too much: → suppressed remodeling.

The desired situation is: Controlled osteoclast activity, rather than: Complete osteoclast suppression.

Future delivery systems could potentially regulate: Dose, Concentration, Duration, location, and Release kinetics.

B. Smart Implant Surfaces

The idea of what a dental implant can be may change from simply being “a mechanically stable titanium implant.” Instead, it could become “a biologically active, programmable implant surface.” This new surface might combine several features, such as osteoconductivity using hydroxyapatite or calcium phosphate. It could also support osteoinduction by using growth factors.

Antimicrobial activity might be achieved with antibacterial coatings. Antiresorptive activity could be provided by bisphosphonates. Controlled release of substances might use nanotechnology or hydrogels. All of these features together could create a multifunctional interface between the implant and bone. However, adding more biological functions also brings new regulatory and safety challenges.

C. Precision Antiresorptive Dentistry

The future of care may focus on precision antiresorptive dentistry. Rather than just asking, "Is this patient taking bisphosphonates?", clinicians can consider, "What is this patient's individual risk-benefit profile?" This profile would include factors such as the drug, dose, duration, disease, bone status, oral infection, procedure, and patient-specific details, resulting in a tailored treatment plan. This method matches the recent shift from broad restrictions to making implant and surgical decisions based on each patient's risk.

Major Current Limitations

Even with recent progress, there are still some important limitations.

- 1. Small clinical studies-** Most of the evidence supporting the use of local bisphosphonates comes from experimental studies or small clinical studies.
- 2. Heterogeneity-** Studies vary in several ways, including the drug used, dose, concentration, delivery method, implant system, and follow-up period.
- 3. Limited long-term evidence-** Long-term safety matters because bisphosphonates can affect the skeleton over time.
- 4. MRONJ remains a major concern-** Any approach that boosts local antiresorptive activity needs to demonstrate that it does not inadvertently increase the risk of osteonecrosis.
- 5. Lack of standardized protocols-** Right now, there is no widely accepted protocol for bisphosphonate-coated implants, local delivery in periodontal treatment, the best concentration, how the drug is released, or how long it should be used locally.

The 2026 systematic review on local bisphosphonate implants highlights this gap in the evidence.

Conclusion

The way bisphosphonates are viewed in dentistry is changing. In the past, most attention focused on the risk of MRONJ. Now, more research is examining how their antiresorptive effects could be used in a controlled, targeted manner. Recent evidence from 2025–2026 shows that patients taking bisphosphonates for osteoporosis do not always need to be excluded from implant treatment, though longer use may slightly raise the risk of MRONJ. One of the most promising areas of research is the development of implant surfaces and delivery systems that use bisphosphonates. However, the latest systematic review finds that there is not yet sufficient evidence to demonstrate that bisphosphonate-coated implants are more effective in practice. Progress in this field will likely depend on using bisphosphonates more precisely, not just in greater amounts. Their role in dentistry may shift from general suppression of bone breakdown to more targeted, personalized bone treatments.

REFERENCES

- 1.Liu H, Wang X, Shi Y, Yang Y, Li P, Chen Q, et al. Dual effects of bisphosphonates on bone metabolism and implant osseointegration: mechanisms, risks and clinical strategies. *J Stomatol Oral Maxillofac Surg.* 2025;126(6S):102534. doi:10.1016/j.jormas.2025.102534.
- 2.Pérez-González F, Sánchez-Labrador L, Sáez-Alcaide LM, López Carriches C, Méniz-García C. Does local bisphosphonate application or surface coating improve implant success? A systematic review. *J Stomatol Oral Maxillofac Surg.* 2026;127(4):102780. doi:10.1016/j.jormas.2026.102780.
- 3.Ali DS, Khan AA, Morrison A, Tetradis S, Mirza RD, El Rabbany M, et al. Antiresorptive therapy to reduce fracture risk and effects on dental implant outcomes in patients with osteoporosis: a systematic review and Osteonecrosis of the Jaw Taskforce consensus statement. *Endocr Pract.* 2025;31(5):686-698. doi:10.1016/j.eprac.2025.02.016.
- 4.Mirza RD, El Rabbany M, Ali DS, Tetradis S, Morrison A, Ruggiero S, et al. Dental implant failure and medication-related osteonecrosis of the jaw related to dental implants in patients taking antiresorptive therapy for osteoporosis: a systematic review and meta-analysis. *Endocr Pract.* 2025;31(9):1189-1196. doi:10.1016/j.eprac.2025.06.003.
- 5.Gangolu M, Jaswitha V, Boyapati R, Dhulipalla R, Maddukuri T, Pasupuleti SC. Bisphosphonates and periodontal health: a systematic review in postmenopausal women. *J Midlife Health.* 2025;16(4):371-385. doi:10.4103/jmh.jmh_120_25.
- 6.Al-Nawas B, et al. Group 3 ITI consensus report: materials and antiresorptive drug-associated outcomes in implant dentistry. *Clin Oral Implants Res.* 2023;34 Suppl 26:169-176.
- 7.Bisphosphonates – boon or bane for oral and maxillofacial surgery? Antiresorptive drugs and their potential role in dentistry and oral and maxillofacial surgery. *J Cranio-Maxillofac Surg.* 2025;53(12):2199-2209. doi:10.1016/j.jems.2025.10.003.