

THE ROLE OF ACETYLSALICYLIC ACID IN ORAL PATHOLOGY: FROM PHARMACODYNAMICS TO CLINICAL MANIFESTATIONS

Kamel Earar^{1,2}, Sondos Al Hamadneh^{3*}, Mariana Lupoae^{1,2}, Caterina Nela Dumitru^{1,2}, Silvia Fotea^{1*}, Cristina Stanescu¹

¹ Faculty of Medicine and Pharmacy, University "Dunarea de Jos" Galati, Romania

² Medical-Pharmaceutical Research Center, Faculty of Medicine and Pharmacy of the "Dunarea de Jos" University of Galați, Romania

³ McMaster University, Ontario, Canada

*Corresponding authors: sondosalhamadneh88@gmail.com , silvia_ghimpu@yahoo.com

All authors have the same contribution.

Abstract

Acetylsalicylic acid (ASA), commonly known as aspirin, is one of the most widely used medications globally due to its analgesic, anti-inflammatory, and antiplatelet effects. While extensively studied in systemic medicine, its implications in oral pathology remain less recognized but are clinically significant. This review explores the role of ASA in the context of oral health, focusing on its pharmacodynamics, local tissue effects, and clinical consequences. ASA can cause various oral manifestations, including mucosal ulcerations, delayed wound healing, and increased bleeding risk during dental procedures. Inappropriate topical use may lead to chemical burns, while systemic use can complicate surgical planning and periodontal management. The review also examines management strategies for dental patients on ASA therapy, highlighting the importance of maintaining therapy in most cases and emphasizing local hemostatic control. Furthermore, the need for future research on ASA's effects on oral tissues, healing, and osseointegration is underscored. A better understanding of these mechanisms can improve dental care quality and patient safety in those receiving ASA therapy.

Keywords: acetylsalicylic acid, oral pathology, bleeding, mucosal lesions, dental surgery

Introduction

Acetylsalicylic acid (ASA), widely known as aspirin, remains one of the most frequently used and studied drugs globally due to its well-established antipyretic, analgesic, anti-inflammatory, and antithrombotic properties. Initially synthesized in the late 19th century, ASA quickly became a staple in systemic therapy, particularly in cardiovascular disease prevention and chronic pain management. Its broad spectrum of indications, accessibility, and affordability contribute to its widespread, often unsupervised use. Despite its systemic efficacy, ASA can exert unintended effects on the oral cavity, both due to systemic circulation and inappropriate local exposure [1-3].

In dentistry, the relevance of ASA transcends pharmacology, affecting clinical protocols, surgical decision-making, and diagnostic pathways. The oral cavity, as a

sensitive and vascularized environment, is particularly susceptible to the pharmacological and toxicological influences of systemically administered drugs. ASA poses unique challenges to dental professionals, ranging from delayed wound healing to increased bleeding risk during oral surgery and adverse mucosal reactions. Although often overlooked, these manifestations may compromise oral health and interfere with standard therapeutic interventions [2-4].

The significance of studying ASA in oral pathology lies in two major dimensions: first, the direct impact on oral tissues through inappropriate use (e.g., chewing or placing ASA tablets directly on the mucosa), which may cause chemical burns, ulcerations, or erosions; and second, the indirect systemic consequences such as bleeding tendencies or delayed mucosal

repair, especially in patients undergoing invasive dental procedures. Moreover, the chronic use of ASA in elderly or polymedicated patients raises concerns about cumulative oral effects, drug interactions, and the modification of standard dental management protocols [1-4].

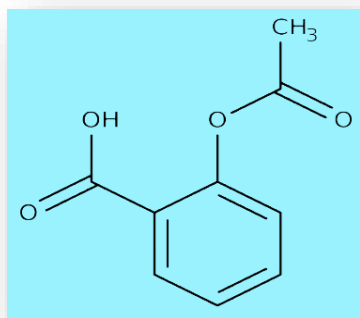


Figure 1. Acetylsalicylic acid (ASA)

Understanding ASA's pharmacodynamics is essential to anticipating and managing its oral effects. As an irreversible inhibitor of the cyclooxygenase enzymes COX-1 and COX-2, ASA reduces prostaglandin and thromboxane synthesis. While this mechanism underlies its therapeutic benefits, it also contributes to the inhibition of platelet aggregation and alteration of inflammatory responses, two mechanisms critically involved in oral tissue repair and hemostasis. Consequently, even low-dose ASA therapy can significantly affect perioperative outcomes in dental surgery, particularly in procedures with a bleeding risk [2-4].

Clinically, ASA has been implicated in a variety of oral lesions, including chemical ulcers, lichenoid-like reactions, burns, and aphthous-like stomatitis, often induced by direct mucosal contact. In some cases, patients may mistakenly apply ASA tablets to painful oral areas, expecting local relief. This misuse may result in epithelial necrosis and localized damage, frequently mistaken for idiopathic or infectious conditions. Additionally, systemic ASA

therapy may exacerbate gingival bleeding, interfere with periodontal therapy, and complicate post-extraction recovery, especially when combined with other anticoagulants or antiplatelet agents [2-5].

In light of these findings, dental practitioners must be aware of the multifaceted role ASA plays in oral pathology. Patient history should include a detailed account of ASA usage, dosage, and method of administration, especially in individuals with unexplained oral lesions or excessive bleeding during dental treatment. Interdisciplinary collaboration is critical, particularly with cardiologists or general physicians managing ASA prescriptions, to balance the thromboembolic risks against surgical bleeding concerns in dental care [1-5].

This review aims to provide a comprehensive synthesis of the literature regarding ASA's influence on oral pathology, starting from its pharmacological foundation to its diverse clinical consequences. By integrating pharmacodynamics with pathophysiological mechanisms and clinical observations, we seek to enhance the dentist's understanding of ASA's dual-edged role in oral health. Identifying and managing ASA-related oral complications can improve patient safety, optimize treatment outcomes, and foster a more holistic, informed approach to dental care in patients undergoing systemic pharmacotherapy [2-6].

Pharmacodynamics and pharmacokinetics of acetylsalicylic acid

Acetylsalicylic acid (ASA), a salicylate derivative, exerts its primary pharmacological effects through irreversible inhibition of cyclooxygenase enzymes (COX-1 and COX-2), which are critical for the biosynthesis of prostaglandins and thromboxanes. This mechanism underlies its analgesic, antipyretic, anti-inflammatory, and antithrombotic properties. The acetylation

of a serine residue in the COX enzymes prevents arachidonic acid from being converted into prostaglandin precursors, reducing both inflammation and platelet aggregation. Inhibition of COX-1, found in most tissues including platelets and gastric mucosa, explains many of ASA's side effects, while COX-2 inhibition accounts more for its anti-inflammatory actions [4-6].

In low doses (typically 75–100 mg/day), ASA primarily acts as an antiplatelet agent by irreversibly inhibiting COX-1 in platelets, leading to reduced thromboxane A₂ production and prolonged bleeding time. Since platelets are anucleated and cannot synthesize new COX enzymes, this effect lasts for the lifespan of the platelet (7–10 days). This antithrombotic action makes ASA a cornerstone therapy for preventing myocardial infarction, stroke, and other thromboembolic events. At higher doses (300–1000 mg), ASA achieves analgesic and antipyretic effects, while anti-inflammatory action typically requires even

greater dosages (over 3000 mg/day), often limited by gastrointestinal toxicity [4-7].

Pharmacokinetically, ASA is rapidly absorbed in the stomach and proximal small intestine. It reaches peak plasma concentrations within 30–60 minutes after oral administration. The acidic pH of the stomach favors passive diffusion of ASA, although enteric-coated formulations can delay absorption to reduce gastric irritation. Once absorbed, ASA undergoes rapid deacetylation in the liver and blood to form salicylic acid, the principal active metabolite, which also contributes to the anti-inflammatory effect. Salicylic acid is subsequently metabolized in the liver through conjugation with glycine or glucuronic acid, then excreted by the kidneys [5-8].

Table 1 summarizes the key pharmacologic characteristics of acetylsalicylic acid (ASA) and their relevance in oral pathology. It highlights systemic effects, administration aspects, and local risks, focusing on clinical challenges in dentistry such as bleeding complications and mucosal damage [4-9].

Table 1. ASA, key pharmacologic and oral implications

<i>Aspect</i>	<i>Details</i>	<i>Relevance in Oral Pathology</i>
<i>Mechanism</i>	Irreversible COX-1 and COX-2 inhibition	↓ Inflammation, ↓ platelet aggregation
<i>Typical doses</i>	75–100 mg (antiplatelet), >300 mg (analgesic)	Bleeding risk in oral surgery
<i>Absorption</i>	Rapid, stomach, and small intestine	Possible gastric irritation → enteric-coated forms
<i>Metabolism</i>	Liver → active salicylate	May affect inflammation and healing
<i>Excretion</i>	Renal (↑ in alkaline urine)	Longer half-life at higher doses
<i>Local toxicity</i>	Direct mucosal application = ulcer/necrosis	Painful chemical lesions, clinically misleading

The drug's elimination half-life is dose-dependent. At low doses, the half-life of ASA is about 20 minutes, while that of

salicylic acid ranges between 2 to 4 hours. At anti-inflammatory doses, metabolism becomes saturated, and the half-life of

salicylate can increase to over 15 hours due to non-linear kinetics. Renal excretion is influenced by urinary pH, with alkaline urine enhancing salicylate elimination [5-9].

From an oral health perspective, these pharmacological properties present both therapeutic benefits and clinical challenges. The irreversible nature of platelet inhibition can significantly increase intraoperative and postoperative bleeding risk in dental procedures. Furthermore, the systemic anti-inflammatory effects of ASA may alter typical inflammatory responses in the oral cavity, potentially delaying the diagnosis of acute lesions or affecting healing trajectories [4,6-10].

Topical exposure, although not recommended, represents a separate mechanism with local toxic effects. ASA applied directly to the oral mucosa—sometimes used by patients seeking localized pain relief—can bypass hepatic metabolism and exert direct chemical injury, leading to mucosal ulceration or necrosis. These events are not related to systemic pharmacokinetics but reflect ASA's low pKa (~3.5) and membrane-permeable form in acidic microenvironments such as inflamed mucosa [7-10].

Understanding the pharmacodynamic and pharmacokinetic profile of ASA is crucial in predicting its potential impact on oral tissues. These mechanisms also form the basis for informed clinical decisions when managing patients on chronic ASA therapy in dental settings [4,6,8-10].

Local effects of acetylsalicylic acid in the oral cavity

Although acetylsalicylic acid (ASA) is primarily administered systemically, it can produce significant local effects in the oral cavity, especially in cases of misuse or chronic exposure. These effects are often underestimated in clinical practice but may lead to a range of soft tissue lesions and

mucosal alterations. The oral cavity is highly vascularized and sensitive to chemical insults, making it particularly susceptible to injury from ASA's acidic and cytotoxic properties when applied directly or inappropriately [7-11].

One of the most commonly reported local adverse effects is ASA-induced chemical burn. Patients occasionally place ASA tablets directly on the oral mucosa—typically on the gingiva, vestibule, or tongue—under the mistaken belief that topical application provides faster pain relief for a toothache or mucosal discomfort. This practice bypasses first-pass metabolism and exposes delicate oral tissues to ASA's acidic environment (pKa ~3.5), leading to localized epithelial necrosis. The result is a sharply demarcated white lesion or ulcer, often painful, with surrounding erythema. Clinically, such lesions may resemble aphthous ulcers, traumatic ulcerations, or even leukoplakia in chronic cases, potentially leading to misdiagnosis [8-11].

Ulcerative lesions caused by ASA are usually self-limiting but can be persistent if the application is repeated or if secondary infection occurs. Histologically, these ulcers show epithelial necrosis with an underlying inflammatory infiltrate. Healing generally occurs within 7–10 days after cessation of exposure, provided no additional trauma or irritation is present. Importantly, a careful patient history is essential to differentiate ASA burns from other ulcerative or precancerous conditions [7,9-11].

Another form of local manifestation is ASA-associated lichenoid reactions, a less frequent but documented hypersensitivity-type response. These lesions typically present as white, reticular, or erosive patches on the buccal mucosa or tongue and may mimic oral lichen planus. Though their pathogenesis is unclear, it is suspected that ASA may trigger a delayed-type immune response in susceptible individuals. Discontinuation of the drug

often leads to lesion resolution, confirming the diagnosis. ASA can also alter the normal healing process of the oral mucosa following trauma or surgery. By interfering with platelet aggregation and inflammatory mediator production, ASA delays clot formation and the early phases of wound repair. Even without overt bleeding, healing may be slower, especially in patients with coexisting conditions like diabetes or in those taking corticosteroids or other NSAIDs [7-11].

In addition, gingival bleeding is a common side effect among patients on low-dose ASA, especially in combination with other anticoagulants. While not always severe, this bleeding may complicate oral hygiene maintenance and periodontal therapy. Patients often report spontaneous bleeding during brushing or flossing, which may be mistaken for signs of active periodontal disease. In surgical contexts, such as tooth extractions or implant placement, ASA therapy requires special consideration, balancing thromboembolic risk with bleeding potential [9-12].

Implications in general oral pathology

Acetylsalicylic acid (ASA) has significant implications in general oral pathology, both through its systemic pharmacological effects and its potential to interfere with local oral conditions. As ASA use is common, particularly among patients with cardiovascular risk, its impact on oral diagnostic, therapeutic, and surgical approaches is becoming increasingly relevant in daily dental practice [6,9-12].

One of the most notable implications is increased bleeding tendency, especially during or after dental procedures. ASA's irreversible inhibition of platelet aggregation alters primary hemostasis, increasing the risk of gingival bleeding, prolonged post-extraction hemorrhage, and bleeding during periodontal therapy or oral surgeries. This risk becomes particularly relevant in patients undergoing procedures involving mucoperiosteal flaps, bone

removal, or multiple extractions. While ASA monotherapy generally does not necessitate treatment discontinuation before minor dental interventions, clinicians must implement appropriate local hemostatic measures, such as suturing, use of hemostatic agents, and compression [10-12].

In chronic ASA users, spontaneous gingival bleeding may be misinterpreted as a sign of active periodontal disease. This can complicate the clinical picture and delay appropriate diagnosis and treatment. Furthermore, in patients with coexisting risk factors, such as vitamin K deficiency, liver dysfunction, or concomitant anticoagulant therapy, the bleeding risk is significantly amplified. Careful history-taking and interdisciplinary communication with the prescribing physician are essential [9-13].

ASA may also modulate the presentation and evolution of common oral pathologies, such as aphthous stomatitis, candidiasis, or traumatic ulcers. Due to its anti-inflammatory effects, ASA can mask the cardinal signs of inflammation, making early diagnosis of infectious or neoplastic lesions more difficult. This is particularly relevant in immunosuppressed patients, where subtle clinical signs may be the first indicators of serious underlying pathology. Additionally, ASA has been implicated in drug-induced oral lesions, including lichenoid reactions and mucosal desquamation. Although rare, these reactions may mimic autoimmune or premalignant disorders, requiring biopsy and histological confirmation. In such cases, identifying ASA as the triggering factor is essential for lesion resolution, typically achieved through drug substitution. [10-13].

ASA use also influences postoperative recovery, particularly in surgical procedures involving soft and hard tissue healing. Impaired platelet function and altered prostaglandin synthesis can delay the initial inflammatory phase of

healing, reducing clot stability and affecting tissue regeneration. In implantology, where early osseointegration is critical, ASA's role remains controversial, with studies showing both neutral and inhibitory effects on bone healing, depending on dosage and duration. ASA therapy intersects with multiple domains of oral pathology. Dentists must be equipped to recognize ASA-related complications, distinguish them from other pathologies, and adapt treatment plans accordingly. Awareness and appropriate risk assessment are key to safe and effective dental care in this patient population [11-13].

Management of the dental patient on acetylsalicylic acid

Managing dental patients undergoing acetylsalicylic acid (ASA) therapy requires a balance between minimizing the risk of bleeding during procedures and avoiding potentially life-threatening thromboembolic events. ASA, especially at low doses (75–100 mg/day), is commonly prescribed for cardiovascular prophylaxis, meaning a significant number of dental patients are continuously exposed to its antiplatelet effects. Therefore, dental professionals must adopt evidence-based strategies to ensure patient safety without compromising treatment outcomes [11-14].

The first step in proper management is comprehensive medical history-taking, including the indication, dosage, and duration of ASA therapy. The dentist should identify whether the patient is on ASA monotherapy or combined antithrombotic treatment (e.g., with clopidogrel or anticoagulants), as the bleeding risk is higher in dual or triple therapy. Coordination with the prescribing physician is crucial before making any decision to interrupt therapy, especially in high-risk patients with a history of myocardial infarction, stroke, or stent placement [8,12-14].

For most minor dental procedures, including single extractions, scaling, and

restorative treatments, the continuation of ASA therapy is generally recommended. Studies show that the risk of thrombosis following ASA discontinuation often outweighs the risk of mild to moderate bleeding, which can typically be controlled with local hemostatic measures. These include the use of absorbable hemostats (oxidized cellulose, collagen sponges), suturing, pressure packs, and tranexamic acid mouthwash [11-14].

In cases of multiple extractions or invasive surgeries, a risk-based approach should be used. Localized interventions, such as staged extractions and atraumatic techniques, help minimize bleeding. In selected cases, and only after medical consultation, temporary cessation of ASA may be considered, but this remains the exception rather than the rule. Patient education is also vital. Patients should be informed of the possibility of prolonged oozing after surgery and instructed on how to manage it at home. Written postoperative instructions and follow-up visits are recommended, especially for elderly or medically complex patients. During the diagnostic phase, clinicians must consider that ASA may cause or worsen gingival bleeding, which can be misinterpreted as advanced periodontal disease. Proper differential diagnosis, supported by probing, imaging, and history, is essential [12-15].

Perspectives and future research directions

Despite its long-standing clinical use, the full impact of acetylsalicylic acid (ASA) on oral health remains underexplored. As ASA continues to be widely prescribed, especially among aging populations with comorbidities, there is a growing need for targeted research that clarifies its role in oral pathology and dental practice [13-15].

One key area requiring further investigation is the dose-dependent influence of ASA on oral wound healing

and tissue regeneration. Current data are mixed, with some studies suggesting delayed healing and others indicating minimal impact, especially at low doses. Research that distinguishes between acute and chronic ASA exposure, and that considers patient-specific variables such as age, smoking status, and systemic conditions, would offer valuable insight into optimal perioperative dental care [12,14-17].

Recent research emphasizes the growing clinical relevance of wisdom tooth inclusion, its correlation with temporomandibular dysfunctions, and the importance of advanced diagnostic imaging such as CBCT in assessing severity. Studies highlight the potential of A-PRF+ in regenerative periodontal therapy, particularly in smokers, and explore the benefits of ceramic-filled composite resins for temporary prosthetics. The effectiveness of dental guards in managing parafunctions and the role of stress-reduction techniques in pediatric anxiety underline a shift toward integrative oral health approaches. These findings point to the need for broader, multidisciplinary investigations that address prevention, precise diagnostics, biomaterials innovation, and patient-centered interventions. Future research should aim to validate these directions through robust clinical trials and long-term outcome assessments [18-25].

Recent studies emphasize the expanding role of biomaterials in oral and systemic rehabilitation. Research on hydrogels, biodegradable polymers, and AI-assisted diagnostics opens promising pathways in tissue engineering and personalized treatment. Innovations in CBCT imaging improve therapeutic decision-making in implantology, while the mechanical behavior of PMMA and ceramic composites suggests durability enhancements for prosthetic solutions [26-32]. The therapeutic applications of phytochemicals, essential oils, and 3D bioprinting indicate a growing

interdisciplinary integration between dentistry, dermatology, and regenerative medicine. Case reports in agenesis rehabilitation and TMJ pathology further highlight the value of precision and biofunctional materials. Future investigations should focus on clinical validation, long-term performance, and the biocompatibility of emerging technologies to ensure their effective integration into routine dental care [29].

Another emerging concern is the local cytotoxicity of ASA when misused topically. While case reports document mucosal burns and ulcerations, there is no standardized protocol for the diagnosis or treatment of such lesions. Future studies should focus on the mechanisms of ASA-induced mucosal damage, the role of pH and tissue permeability, and potential protective measures to prevent patient self-misuse.

Pharmacogenetics and personalized medicine also present new frontiers. Understanding individual variability in ASA metabolism, platelet sensitivity, and mucosal response may lead to safer, tailored dental protocols. This could be particularly useful in patients on dual or triple antithrombotic therapy, where bleeding risk is significantly elevated.

In implantology and oral surgery, research is needed to determine whether ASA influences osseointegration and bone healing. While systemic anti-inflammatory action may theoretically impair early healing phases, some studies suggest potential benefits through modulation of chronic inflammation. Interdisciplinary collaboration should be emphasized. Clearer guidelines for managing ASA-treated patients during dental procedures, based on robust clinical trials, would aid both dentists and physicians in decision-making, avoiding unnecessary treatment interruptions or complications.

Conclusion

Acetylsalicylic acid (ASA) plays a significant dual role in dentistry, providing systemic therapeutic benefits while posing notable risks to oral health. Its pharmacodynamic properties, particularly the irreversible inhibition of platelet aggregation and modulation of inflammation, have direct implications in oral pathology and dental procedures. ASA can contribute to mucosal lesions, delayed wound healing, and increased bleeding, especially when used improperly or in conjunction with invasive treatments. Despite these risks, ASA discontinuation is rarely justified and may endanger patients

with cardiovascular conditions. Therefore, proper patient evaluation, individualized treatment planning, and effective communication with physicians are essential. Dentists must be vigilant in identifying ASA-related complications and apply appropriate local hemostatic measures. Further research is needed to establish clear clinical protocols and to deepen our understanding of ASA's interaction with oral tissues. In summary, a balanced, evidence-based approach ensures safe and effective dental care for patients on ASA therapy.

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