

ACETYLSALICYLIC ACID IN CARDIOLOGY: BENEFITS, RISKS, AND CLINICAL INDICATIONS

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Abstract

Acetylsalicylic acid (ASA) is an antiplatelet agent widely used in cardiology and has an essential role in the prevention and treatment of cardiovascular diseases. By irreversibly inhibiting cyclooxygenase-1 (COX-1), ASA reduces platelet aggregation and the risk of thrombotic events, being recommended in the secondary prevention of myocardial infarction, stroke, and peripheral arterial disease. It is also a central element in the treatment of acute coronary syndromes, administered in combination with other antiplatelet agents. However, its use is not without risks, the main adverse effects being gastrointestinal and intracranial hemorrhages. In primary prevention, the benefits are questionable, requiring a careful evaluation of the risk-benefit ratio. Current research is exploring strategies for optimizing the administration of ASA, including dose adjustment, intermittent administration, and identifying biomarkers that allow for personalized use. The development of safer alternatives and innovative formulations could improve the safety profile of ASA in the future. Thus, individualization of treatment remains essential to maximize efficiency and reduce associated risks.

Keywords: Acetylsalicylic acid, cardiology, cardiovascular prevention, acute coronary syndromes, antiplatelet therapy, hemorrhagic risks.

Introduction

Acetylsalicylic acid (ASA), commonly known as aspirin, is one of the most widely used drugs in the world, with a long history in medical practice. Discovered in the late nineteenth century, ASA is derived from salicylic acid and was originally used as an analgesic and antipyretic agent. Subsequently, research highlighted its anti-inflammatory and antiplatelet properties, prompting the expansion of its use in the prevention and treatment of cardiovascular diseases. Its mechanism of action is based on the inhibition of cyclooxygenase (COX-1 and COX-2), which leads to a reduction in the synthesis of prostaglandins and thromboxane A₂, an essential factor in platelet aggregation. This irreversible

inhibition of COX-1 prevents blood clots, reducing the risk of thrombotic events [1-3].

In cardiology, ASA has become a fundamental pillar in the primary and secondary prevention of cardiovascular diseases. In primary prevention, the administration of ASA aims to reduce the risk of developing a first major cardiovascular event, such as myocardial infarction or stroke, in patients with risk factors such as diabetes, hypertension, dyslipidemia, or a family history of cardiovascular disease. Clinical trials, such as ASPREE and ARRIVE, have raised questions about the actual benefits of ASA in primary prevention, highlighting an increased risk of bleeding that could

outweigh the benefits in patients at low risk of cardiovascular events [1-4].

In secondary prevention, ASA is widely used to reduce the risk of recurrence of ischemic events in patients with a history of myocardial infarction, ischemic stroke, angina pectoris, or peripheral arterial disease. The benefits of chronic stewardship in this context are well documented and supported by the current guidelines of the European Society of Cardiology (ESC) and the American Heart Association (AHA), which recommend the use of ASA at doses between 75-100 mg/day for secondary prevention in patients with documented atherosclerotic disease [2-4].

Another area where ASA plays a key role is the treatment of acute coronary syndromes (ACS). In patients with ST-segment elevation acute myocardial infarction (STEMI) or non-ST-segment elevation (NSTEMI), prompt

administration of a loading dose of 150-300 mg of ASA followed by a daily maintenance dose is a standard intervention. The combination with other antiplatelet agents, such as clopidogrel, ticagrelor, or prasugrel, in double or triple antiplatelet therapy, optimizes the prevention of thrombosis and improves the prognosis of post-infarction patients [2-5].

Although the effectiveness of ASA in the prevention and treatment of cardiovascular diseases is undeniable, its use is not without risks. Among the most common adverse effects is the increased risk of gastrointestinal and intracranial hemorrhages, which can have severe consequences, especially in elderly patients or those undergoing concomitant anticoagulant therapy. Concomitant administration of proton pump inhibitors (PPIs) is often recommended for patients at high risk of gastro-duodenal ulcers [3-6].

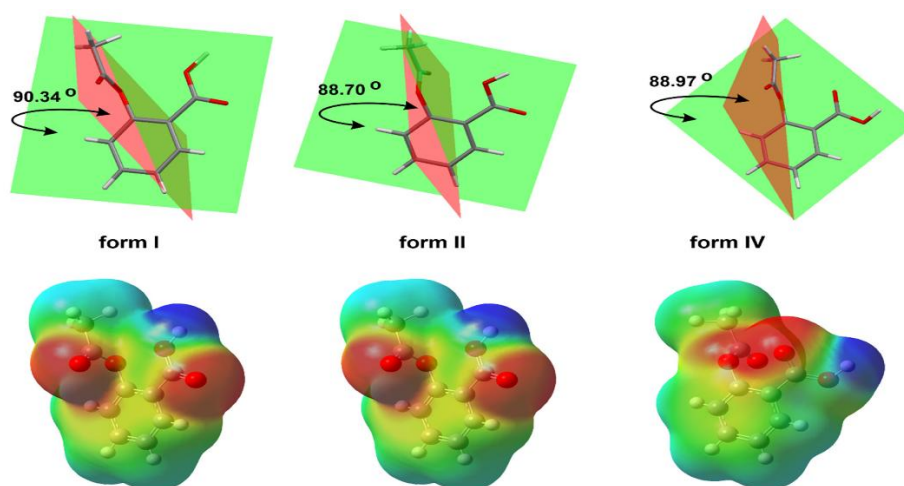


Figure 1. The fundamental crystal structure of acetylsalicylic acid (ASA) is represented by the CSD refcode ACSALA. A comparative 3D molecular analysis of its polymorphic forms I (ACSALA), II (ACSALA13), and IV (ACSALA24) reveals distinct orientations of the hydroxyl (-OH) and acetyl (-Ac) groups. In forms I and II, the -OH group is positioned on the same side relative to the -Ac group, whereas in form IV, an inverse spatial arrangement is observed. Additionally, a computed molecular electrostatic potential map highlights the charge distribution across the different ASA polymorphs [6].

In addition to its use in cardiovascular disease, recent research suggests other possible beneficial effects of ASA, including in the prevention of some cancers, such as colorectal cancer, through mechanisms that involve inhibiting inflammation and cell proliferation. However, its use for this purpose remains controversial and requires further studies to establish the precise indications [2,4-6].

Benefits of acetylsalicylic acid in cardiology

Acetylsalicylic acid (ASA) is an essential drug in cardiology due to its antiplatelet properties, which reduce the risk of arterial thrombi formation. Its main mechanism of action consists in the irreversible inhibition of cyclooxygenase-1 (COX-1), the enzyme responsible for the production of thromboxane A₂, a pro-platelet aggregator mediator. Through this inhibition, ASA prevents platelet aggregation, decreasing the risk of thrombosis and reducing the incidence of major cardiovascular events [2,4-6].

The role of ASA in primary prevention is controversial, but in certain

categories of patients, it can bring significant benefits. Studies such as ASPREE and ARRIVE have suggested that the use of ASA in patients with no history of cardiovascular events should be carefully individualized. In patients with high cardiovascular risk (diabetes, hypertension, dyslipidemia) but no history of myocardial infarction or stroke, ASA may reduce the risk of these events. However, the benefits must be weighed against the risk of bleeding, which may outweigh the cardiovascular benefits in some cases [4-7].

ASA has an established role in the secondary prevention of cardiovascular disease. In patients with acute myocardial infarction (AMI), ischemic stroke, or peripheral arterial disease, daily administration of a low dose of ASA (75-100 mg) significantly reduces the risk of recurrence of thrombotic events. Studies such as ISIS-2 and the Antithrombotic Trialists' Collaboration have demonstrated an approximately 25% reduction in cardiovascular mortality and non-fatal myocardial infarction in patients receiving ASA in secondary prevention [4-8].

<i>Benefit category</i>	<i>Mechanism of action</i>	<i>Clinical evidence</i>
<i>Antiplatelet effect</i>	Irreversible inhibition of COX-1, reducing thromboxane A ₂ production, preventing platelet aggregation.	Demonstrated in multiple trials (e.g., ISIS-2, Antithrombotic Trialists' Collaboration).
<i>Primary prevention</i>	Reduces the risk of first-time myocardial infarction (MI) in high-risk individuals, although with debated effectiveness.	Conflicting results; studies like ASPREE and ARRIVE suggest benefits depend on patient risk profile.
<i>Secondary prevention</i>	Significantly lower the recurrence of MI, stroke, and cardiovascular mortality in patients with a history of cardiovascular events.	Robust evidence from studies like CAPRIE, CURE, and COMPASS confirm significant risk reduction.
<i>Acute coronary syndrome (ACS) management</i>	Immediate use in ACS reduces mortality; and enhances efficacy when combined with P2Y ₁₂ inhibitors.	Essential in STEMI/NSTEMI management; early administration linked to reduced mortality in trials like ISIS-2.

<i>Stroke prevention</i>	Prevents recurrent ischemic strokes and transient ischemic attacks (TIA) by reducing thrombus formation.	Proven efficacy in stroke prevention as recommended by AHA and ESC guidelines.
<i>Peripheral arterial disease (PAD)</i>	Improves blood flow by preventing clot formation in narrowed arteries, reducing limb ischemia and amputation risk.	Supported by CAPRIE trial showing benefits in PAD patients for reducing cardiovascular events.
<i>Anti-inflammatory and atherosclerosis prevention</i>	Reduces systemic inflammation and stabilizes atherosclerotic plaques, lowering the risk of plaque rupture.	Emerging data suggest anti-inflammatory properties contribute to reducing cardiovascular risk.
<i>Long-term cardiovascular protection</i>	Provides continuous cardiovascular event risk reduction with long-term daily low-dose administration.	Meta-analyses confirm sustained risk reduction over the years, especially in secondary prevention.
<i>Potential synergy with other therapies</i>	Enhances the effects of statins, anticoagulants, and lifestyle modifications, optimizing cardiovascular protection.	Combining aspirin with other cardioprotective agents improves overall outcomes, per ACC/AHA guidelines.
<i>Cost-effectiveness and accessibility</i>	Widely available, low-cost therapy with strong clinical evidence supporting its benefits in cardiovascular disease management.	Cost-effective intervention for reducing cardiovascular morbidity and mortality globally.

Table 1. The table summarizes the key benefits of acetylsalicylic acid (Aspirin) in cardiology, detailing its antiplatelet effects, role in primary and secondary prevention, and impact on conditions such as acute coronary syndrome, stroke, and peripheral arterial disease. It also highlights its anti-inflammatory properties, long-term cardiovascular protection, clinical evidence, and potential synergy with other therapies [2-10].

In acute coronary syndromes, ASA is a first-line treatment. Administration of a loading dose of 150-300 mg, followed by a maintenance dose of 75-100 mg/day, is essential for the prevention of thrombosis in the affected artery. The combination with a P2Y₁₂ receptor inhibitor (clopidogrel, ticagrelor, prasugrel) in dual antiplatelet therapy is standard in the management of ACS. This combination significantly reduces the risk of major ischemic events, including recurrent myocardial infarction and cardiovascular death [5-9].

In patients with peripheral artery disease, ASA is used to prevent arterial thrombosis and critical limb ischemia. Also, in patients with a history of ischemic stroke or transient ischemic attack (TIA), ASA reduces the risk of recurrence of

cerebrovascular events. Studies such as CAPRIE have demonstrated that ASA has a clear protective effect on patients with documented atherosclerosis [6-10].

Risks and adverse effects of acetylsalicylic acid

Acetylsalicylic acid (ASA) is an essential drug in cardiology, but its use is not without risks and adverse effects, the most important of which are hemorrhagic and gastrointestinal. Its mechanism of irreversible inhibition of cyclooxygenase-1 (COX-1) reduces the production of thromboxane A₂, preventing platelet aggregation, but also affects the synthesis of protective prostaglandins in the gastric mucosa, increasing the risk of digestive damage. The most common adverse effect of ASA is gastrointestinal bleeding, which

ranges from erosive gastritis to hemorrhagic or perforated ulcers. Patients with a history of peptic ulcer disease or concomitant treatment with non-steroidal anti-inflammatory drugs (NSAIDs) are at increased risk, and proton pump inhibitors (PPIs) are recommended for gastric protection [4,7-10].

Another major adverse effect of ASA is intracranial hemorrhage, which, although rare, can have devastating consequences. The risk increases with age, uncontrolled high blood pressure, and concomitant use of oral anticoagulants or other antiplatelet agents. Studies have shown that chronic administration of ASA can increase the risk of hemorrhagic stroke, especially in patients without a clear indication for antiplatelet therapy. Therefore, the benefits must be carefully weighed against the risks, especially in primary prevention, where the cardiovascular protective effect may be lower than the risk of bleeding [7-10].

In some people, ASA can induce allergic reactions, manifested by rashes, bronchospasm, or anaphylaxis. Patients with asthma or NSAID intolerance may develop a hypersensitivity reaction known as Samter syndrome, characterized by the asthma triad, nasal polyposis, and aspirin intolerance. In these cases, the administration of ASA is contraindicated, and therapeutic alternatives must be carefully evaluated [5,7-10].

Another important adverse effect is Reye's syndrome, a rare but serious condition that affects children and adolescents treated with ASA in the context of viral infections such as influenza or chickenpox. Reye's syndrome causes acute liver dysfunction and severe encephalopathy and being associated with

high mortality. For this reason, ASA is strictly contraindicated in children under 16 years of age, and safe alternatives, such as paracetamol, are preferred for the treatment of fever and pain in this category of patients [4,7-10].

Drug interactions are another important aspect of the use of ASA. Concomitant administration with oral anticoagulants, such as warfarin or new oral anticoagulants (NOACs), increases the risk of major bleeding, requiring close monitoring. Also, the combination with other non-steroidal anti-inflammatory drugs can potentiate the gastrototoxic and hemorrhagic effects, and the concomitant use of corticosteroids increases the risk of gastric ulcers. In patients with chronic kidney disease, ASA may worsen renal failure by reducing renal perfusion, and in patients with hepatic impairment, it may increase the risk of bleeding due to impaired clotting function [8-10].

Clinical indications and user guides

The use of acetylsalicylic acid (ASA) in cardiology is guided by clear clinical indications, established based on scientific evidence and international recommendations. In the primary prevention of cardiovascular disease, the administration of ASA is controversial and must be individualized. Recent studies, such as ASPREE and ARRIVE, have shown that the benefits of ASA in the prevention of the first cardiovascular event are modest and may be outweighed by the risk of major bleeding, especially in patients without significant cardiovascular risk factors. Current guidelines do not recommend routine administration of ASA for primary prevention, but it may be indicated in patients at very high

cardiovascular risk, such as those with diabetes, severe hypertension, or a family history of premature cardiovascular events, after careful risk-benefit assessment [7-11].

In secondary prevention, the use of ASA is well established and supported by multiple clinical trials that have demonstrated a significant reduction in cardiovascular mortality and the risk of recurrent myocardial infarction or stroke. Patients with documented atherosclerotic disease, including those with a history of myocardial infarction, stable or unstable angina, ischemic stroke, or peripheral artery disease, should receive ASA in low doses, usually between 75-100 mg daily. Long-term administration has been associated with a reduction in recurrent thrombotic events, but it should be closely monitored to prevent bleeding complications [5,8-12].

In acute coronary syndromes (ACS), ASA is an essential element of initial and long-term treatment. Patients with ST-segment elevation acute myocardial infarction (STEMI) or without ST-segment elevation (NSTEMI) should receive a loading dose of 150-300 mg, followed by a maintenance dose of 75-100 mg per day. It should be administered in combination with a P2Y₁₂ receptor inhibitor, such as clopidogrel, ticagrelor, or prasugrel, for at least 12 months in patients who have undergone coronary angioplasty revascularisation with stent implantation. After this period, dual antiplatelet therapy is reduced to ASA monotherapy, if the thrombotic risk remains low [8-12].

For patients with ischemic stroke or transient ischaemic attack, ASA is recommended for the secondary prevention of recurrences. The doses used range between 75-100 mg/day, and in certain

situations, it may be combined with clopidogrel for a limited period, especially in the first weeks after a minor stroke or TIA, to reduce the risk of subsequent vascular events [6,8-12].

The administration of ASA should be adjusted according to the characteristics of the patient. In the elderly, the risk of gastrointestinal and intracranial bleeding is higher and the decision to continue treatment should be based on a careful risk-benefit assessment. Patients with advanced renal impairment may have an increased risk of complications because ASA can affect glomerular filtration, and in patients with severe liver failure, the risk of bleeding is accentuated due to impaired coagulation [8-13].

International guidelines, including those of the European Society of Cardiology (ESC) and the American Heart Association (AHA), emphasize the importance of personalized use of ASA. Treatment decisions should be made based on the individual risk profile, and in patients at increased bleeding risk, risk reduction strategies should be considered, such as combination with proton pump inhibitors for gastric protection or dose adjustment [8-14].

Future perspectives and new research directions

Although acetylsalicylic acid (ASA) remains an essential pillar in the prevention and treatment of cardiovascular disease, current research focuses on optimizing its use and identifying safer and more effective alternatives. One of the major directions of research aims to individualize therapy by using biomarkers and predictive models to select patients who benefit most from ASA while

reducing the risk of bleeding complications. Genetic studies explore the polymorphisms that influence the response to ASA, and platelet function tests are investigated as potential methods for guiding personalized antiplatelet therapy [9-14].

Another important direction is to identify optimal doses of ASA for various categories of patients. Studies suggest that a lower than standard dose of 75-100 mg/day could provide similar cardiovascular protection, but with a lower bleeding risk. There is also interest in intermittent administration, instead of daily administration, to reduce adverse effects. This strategy could be particularly beneficial in elderly patients or those with multiple comorbidities [9-15].

Research on alternatives to ASA is constantly developing. Selective COX-2 inhibitors, such as celecoxib, are being investigated for their potential to maintain the antiplatelet effects of ASA, but with a lower bleeding risk. Other options, such as inhibition of non-TXA2 platelet activation pathways, could lead to the development of therapies with a higher safety profile. Also, the combination of ASA with other vascular protective agents, such as statins or antioxidants, is being analyzed to determine whether this approach can improve cardiovascular prognosis without increasing the risks associated with antiplatelet therapy [6,9-16].

Acetylsalicylic acid (ASA) is an essential antiplatelet agent in the prevention and treatment of cardiovascular disease, reducing the risk of thrombotic events. However, its use can be associated with bleeding risks, and complementary alternatives, such as essential oils, are being studied for their antioxidant and anti-

inflammatory effects. Lavender, peppermint, geranium, and rosemary oils may help reduce oxidative stress and regulate blood pressure, complementing the therapeutic effects of ASA. Although promising, these approaches require further research to determine the efficacy and safety of their use alongside conventional antiplatelet therapy in oral rehabilitation [17-21].

Acetylsalicylic acid (ASA) is essential in the prevention of cardiovascular diseases, having an antiplatelet effect, but it also presents hemorrhagic risks, which are also relevant in dentistry. In the case of extraction of impacted teeth, the use of ASA increases the risk of postoperative bleeding, requiring adjustment of the treatment to avoid complications. On the other hand, inflammation caused by impacted teeth can favor systemic responses that affect cardiovascular health. Therefore, the management of patients with antiplatelet therapy and indication for extraction of impacted teeth should be personalized to balance cardiovascular benefits and hemorrhagic risk [22-33].

Acetylsalicylic acid (ASA) is essential in the prevention of cardiovascular disease, but the risk of bleeding requires exploring alternatives. Advanced biomaterials, such as hydrogels and controlled-release nanoparticles, could optimize the administration of ASA, reducing adverse effects. In cardiology, stents coated with bioactive biomaterials improve the prevention of thrombosis, and in dentistry, osteoconductive biomaterials facilitate post-extraction bone regeneration in patients undergoing antiplatelet therapy. Biomaterials research promises innovative solutions, minimizing the risks of ASA and

maximizing the benefits, opening up new perspectives for safer and more effective treatments in cardiovascular and dental medicine [34-45].

Another important aspect is to optimize the duration of treatment with ASA in combination with other antiplatelet agents, such as clopidogrel, ticagrelor, or prasugrel. Recent studies suggest that, in certain categories of patients, a shorter duration of dual antiplatelet therapy may reduce the risk of bleeding without compromising cardiovascular protection. This approach could be particularly beneficial in patients at increased bleeding risk, such as those with a history of gastrointestinal bleeding or chronic renal failure [46-50].

New technologies in pharmaceutical development could lead to advanced controlled-release ASA formulations that reduce the risk of bleeding while maintaining the cardiovascular protective effect. Also, combined administration with protective agents of the gastric mucosa, such as synthetic prostaglandins, is being analyzed to reduce the risk of ulcers and digestive bleeding [50-58].

Conclusions

Acetylsalicylic acid remains an essential medicine in cardiology, having proven benefits in the prevention and treatment of cardiovascular diseases. Its use in the secondary prevention of ischemic events is well documented, significantly reducing the risk of recurrent myocardial infarction, stroke, and other

thrombotic complications. Also, its role in acute coronary syndromes is undeniably part of the standard treatment recommended by international guidelines.

However, the use of ASA is not without risks, the most important being gastrointestinal and intracranial hemorrhages, which can have serious consequences, especially in elderly patients or those with multiple comorbidities. For this reason, the decision to take it must be individualized, taking into account both the cardiovascular benefits and the associated risks. In primary prevention, its use must be carefully evaluated, and in many cases, non-pharmacological strategies or other therapeutic interventions may be preferred to reduce cardiovascular risk.

Future research aims to optimize the use of ASA by identifying strategies to reduce bleeding risk, such as dose adjustment, intermittent administration, or combination with gastroprotective agents. In addition, the development of safer alternatives, including new classes of antiplatelet agents or advanced formulations of ASA, could improve treatment effectiveness without compromising patient safety.

ASA continues to be a core therapeutic tool in cardiology, but its use must be guided by sound scientific evidence and tailored to each patient's profile. In the context of a modern and evidence-based approach to antiplatelet therapy, careful monitoring and personalization of treatment remain essential to maximize benefits and reduce risks.

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