Aspirin's Centenary Journey: From a Historic Discovery to a Cornerstone of Modern Medicine

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***Abstract*—This study reviews the developmental history of aspirin (Fig. 1), its clinical applications and adverse reactions, and analyses current research challenges to provide a reference for its rational clinical use. Relevant literature on aspirin's origin, synthesis, mechanism, and clinical research was comprehensively combed and summarized. Aspirin exerts antipyretic, analgesic, anti-inflammatory and antiplatelet effects by irreversibly inhibiting Cyclooxygenase (COX) activity. It is a core drug for cardiovascular and cerebrovascular disease prevention, and has potential value in gastrointestinal cancer prevention, pre-eclampsia prophylaxis, and Kawasaki disease treatment. However, it has adverse reactions such as gastrointestinal irritation, and aspirin resistance limits its clinical application. Aspirin is a typical representative of the integration of traditional medicine and modern science, and it still occupies an important position in clinical practice after a century of development. In the future, research on aspirin should focus on personalized precision medication, the development of safer formulations, the exploration of new indications, and the in-depth excavation of its non-COX pathway mechanisms, which will further unlock its clinical value and bring more benefits to human health.**

***Keywords*—aspirin, acetylsalicylic acid, developmental history, clinical application, adverse reaction, aspirin resistance**

I. Introduction

Throughout the long history of medicine, few drugs have enjoyed such enduring popularity as aspirin. The renowned philosopher José Ortega y Gasset aptly captured its unique value when he said: 'If I were stranded on a desert island and had to choose a single medicine to take with me, the first thing that would come to mind would be aspirin!' Also known as Acetylsalicylic Acid (ASA), it is an organic compound with the chemical formula (C9H8O4), used as an antipyretic, analgesic, Non-Steroidal Anti-Inflammatory Drug (NSAID), and antiplatelet agent [1].

Its story began with humanity's observation of nature, was shaped by the ingenuity of chemists, and flourished through pharmacologists' exploration of its mechanisms. Since its inception, it has held a significant position in the medical field due to its remarkable efficacy and relatively good safety profile [2]. The development of aspirin spans thousands of years, from the ancient use of willow bark to the artificial synthesis of acetylsalicylic acid, and to the clarification of its molecular mechanism and the expansion of clinical indications; each stage is a reflection of the progress of medical science [3].

Understanding the development history of aspirin helps us better comprehend the scientific principles of drug development; exploring its clinical applications, in turn, allows us to fully grasp the value and limitations of this classic drug in the prevention and treatment of diseases [4]. This paper reviews aspirin's developmental history, clinical applications and adverse reactions, and analyses current research challenges, providing a theoretical basis for its rational clinical use and in-depth research.

II. The History of Aspirin's Development

A. *Ancient Origins and Early Applications*

The medicinal history of salicylic acid, aspirin's parent compound, dates to ancient times. As early as 1534 BC, the Ebers Papyrus, ancient Egypt's earliest medical text, recorded willow bark and leaves for anti-inflammatory and analgesic use [1]. In 400 BC, Hippocrates used willow leaf tea to relieve childbirth pain and reduce fever [2]. For millennia, willow bark served as a natural remedy for pain and fever, though its active components and mechanisms remained unknown, with use based solely on empirical experience [5].

B. *Scientific Investigation and Component Separation*

By the early 19th century, the active components of willow bark were gradually identified. In 1828, Joseph Buchner first isolated a yellow crystalline active compound from willow bark, named salicin [2]. Shortly afterwards, Raffaele Piria isolated a more potent compound, salicylic acid, from these crystals [2]. In 1852, Charles Gerhart discovered salicylic acid's molecular structure, though his synthetic product was unstable. By 1859, Hermann Kolbe achieved artificial chemical synthesis of salicylic acid [3], enabling its widespread use for pain and inflammation. However, its bitter taste, severe gastric mucosal irritation, and poor patient tolerance limited its clinical application.

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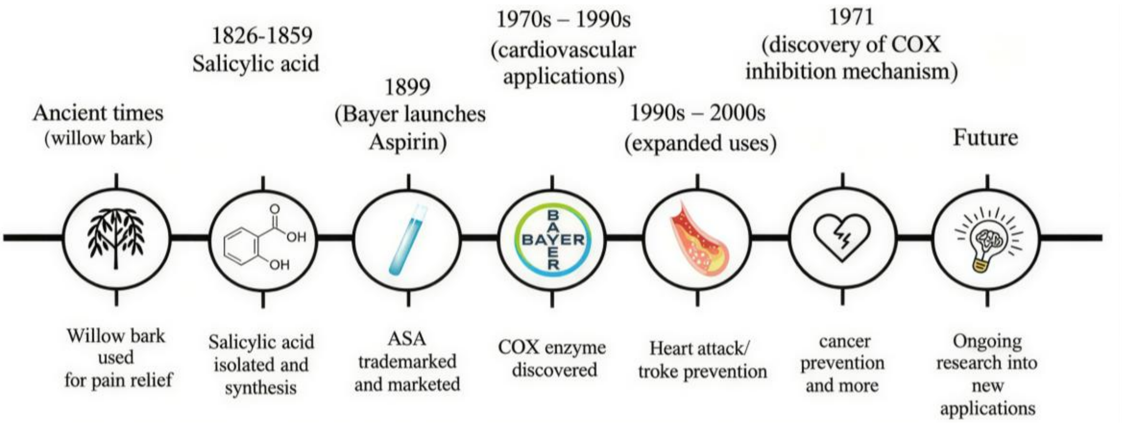

Fig. 1. Timeline of Aspirin development.

C. Key Breakthroughs and Synthetic Drug

To address salicylic acid's drawbacks, scientists pursued structural modifications (Fig. 1). In 1897, Bayer chemist Felix Hoffman, seeking gentler treatment for his father's rheumatoid arthritis, synthesized highly pure, stable acetylsalicylic acid by modifying salicylic acid. This compound retained salicylic acid's therapeutic efficacy while reducing gastrointestinal irritation [4]. Bayer quickly recognized the immense value of this discovery and registered the trade name 'Aspirin' ('A' stands for acetyl, 'spir' comes from the Latin name for spiraea, Spiraea, which is another natural source of salicylic acid, and 'in' was a suffix commonly used for medicines at the time). Thanks to its exceptional efficacy and improved tolerability, it quickly gained popularity worldwide, becoming the world's first truly synthetic drug and the first over-the-counter painkiller to be launched.

D. Elucidation of the Mechanism of Action

In 1971, John Vane elucidated aspirin's core mechanism, discovering it inhibits prostaglandin synthesis [2]—substances linked to pain, fever, inflammation and platelet aggregation, unravelling its action mystery. Further studies revealed aspirin irreversibly inhibits Cyclooxygenase-1 (COX-1), reducing Thromboxane A2 (TXA2), a potent vasoconstrictor and platelet aggregation stimulator, proving it an effective anti-thrombotic agent [2]. Clinical trials confirmed aspirin reduces mortality from myocardial infarction [5] and stroke [6], opening its use in cardiovascular and cerebrovascular disease treatment. Vane was awarded the 1982 Nobel Prize in Physiology or Medicine.

III. Clinical Application of Aspirin

A. Traditional Uses

1) Antipyretic and analgesic

Aspirin is a classic antipyretic and analgesic drug, which is widely used for fever caused by colds, flu, and various infectious diseases; it is also effective for moderate pain such as headaches, toothaches, muscle aches, neuralgia, and dysmenorrhoea [2]. Its antipyretic mechanism is to inhibit the synthesis of prostaglandins in the hypothalamic temperature regulation center, reset the temperature set point, and make the body temperature return to normal through sweating and heat dissipation [7]. Its analgesic effect is mainly aimed at inflammatory pain, by inhibiting the synthesis of prostaglandins at the pain site, reducing the sensitization of nerve endings to pain-causing substances such as bradykinin, and thus relieving pain [8].

As aspirin inhibits the synthesis of prostaglandins in the uterus, it can effectively relieve menstrual pain. Aspirin is safe and inexpensive; it is generally most effective when taken three days prior to the onset of menstruation [7]. It should be taken after meals to avoid irritation of the gastrointestinal tract, and it is not suitable for individuals with allergies, asthma, peptic ulcers, poor blood clotting, or those who have recently undergone surgery [2].

2) Anti-inflammatory and anti-rheumatic

Aspirin is one of the fundamental drugs for the treatment of rheumatic fever, rheumatic arthritis, and rheumatoid arthritis, and can effectively alleviate symptoms of joint redness, swelling, heat, and pain [8]. The core mechanism involves inhibiting the activity of Cyclooxygenase (COX-1 and COX-2) in inflammatory tissues, blocking the conversion of arachidonic acid into Prostaglandins (PGs) by irreversibly acetylating the active sites of the enzymes [8]. Prostaglandins are key mediators of the inflammatory response; reducing their production inhibits the transmission of inflammatory signals at the source, thereby exerting anti-inflammatory and anti-rheumatic effects [2].

Specifically, it significantly alleviates the four classic local symptoms of inflammation: 'redness, swelling, heat and pain' [8]. For instance, during the acute phase of rheumatic fever, it rapidly relieves congestion, oedema and pain in joints and soft tissues, and is the first-line drug for the symptomatic treatment of acute rheumatic fever [2]. For rheumatoid arthritis, it can effectively improve symptoms of joint pain and swelling in patients and enhance joint mobility [8]. It should be noted, however, that this effect is purely symptomatic; it cannot cure the disease nor halt the progression of damage to joint cartilage and bone tissue, and it needs to be combined with disease-modifying antirheumatic drugs for long-term treatment [8].

B. Modern Core Applications

- Prevention and treatment of cardiovascular and cerebrovascular diseases

The antiplatelet effect of aspirin is its most important clinical application in modern medicine, which has completely changed the prevention and treatment pattern of cardiovascular and cerebrovascular diseases [1]. Aspirin irreversibly inhibits the COX-1 activity in platelets, thereby reducing the production of TXA2—a substance that strongly promotes platelet aggregation and vasoconstriction—effectively inhibiting platelet aggregation and preventing the formation of blood clots [6]. This represents the most significant shift in the clinical application of aspirin, moving from 'treating existing conditions' to 'preventing future conditions' [4].

Primary prevention: For individuals who have not yet experienced a cardiovascular event but possess high-risk factors (such as hypertension, diabetes, hyperlipidaemia, smoking, obesity and a family history of cardiovascular diseases), the use of aspirin requires a rigorous risk-benefit assessment [9]. As the benefits of preventing cardiovascular events may be offset by an increased risk of bleeding (particularly gastrointestinal bleeding), current clinical guidelines tend to be cautious, recommending its use only for specific high-risk individuals with a low risk of bleeding [9]. Low-dose aspirin (75–100 $mg \cdot d^{-1}$) is the recommended dosage for primary prevention [9].

Secondary prevention: For patients with established atherosclerotic cardiovascular disease (such as myocardial infarction, stable or unstable angina, ischemic stroke, transient ischemic attack, or peripheral arterial disease), long-term low-dose aspirin is the standard treatment regimen and significantly reduces the risk of recurrence and mortality [10]. A large number of randomized controlled trials have confirmed that long-term aspirin use can reduce the relative risk of recurrent cardiovascular events in these patients by about 25% [10]. The recommended dosage for secondary prevention is 75–150 $mg \cdot d^{-1}$, and individualized adjustment can be made according to the patient's tolerance [6].

C. Potential and Emerging Applications

1) Cancer prevention

Extensive epidemiological and clinical data indicate that long-term regular low-dose aspirin use is associated with reduced risk and mortality of colorectal and other gastrointestinal cancers [11]. Its anti-tumor mechanism involves multiple pathways: inhibiting the COX pathway to suppress prostaglandin synthesis, reducing Bcl-2 expression to induce cancer cell apoptosis, and inhibiting tumor angiogenesis to weaken invasion and metastasis [11], with significant effects on gastrointestinal cancers including colorectal, esophageal and Gastric Cancer (GC) [11].

GC is a highly prevalent, fatal malignancy worldwide, with advanced patients having a median survival of less than 12 months [11]. Current GC treatment, centered on surgery combined with chemo-, radio-, targeted and immunotherapy, has unsatisfactory efficacy, shifting research focus to early prevention [11]. Serum Pepsinogen I (PGI) and II (PGII) assess gastric mucosal function for GC high-risk screening [11]. Long-term aspirin administration for 1 year can elevate the PGI/PGII ratio and partially reverse gastric mucosal atrophy under endoscopy in patients with chronic atrophic gastritis (CAG, a GC precancerous lesion), suggesting aspirin improves gastric mucosal function and reduces GC risk [9, 11].

Aspirin also prevents Hepatocellular Carcinoma (HCC), the most common primary liver cancer (75%–85% of primary liver cancers) [12]. In China, primary liver cancer ranks 5th in incidence and 2nd in mortality [12]. The NIH-Retirees' Association Diet and Health Study first showed 41% lower HCC risk in aspirin users [12]. The mechanism involves inhibiting glycolysis: aspirin suppresses Enolase 1 (ENO1), a key glycolytic enzyme, to block HCC cell energy metabolism and proliferation in the hypoxic tumor microenvironment [12].

2) Prevention of pre-eclampsia

Pre-eclampsia is a hypertensive disorder specific to pregnancy, characterized primarily by elevated blood pressure and proteinuria after 20 weeks of gestation; it is one of the leading causes of maternal and perinatal mortality [13]. In China, the incidence of pre-eclampsia ranges from 2.6% to 5.1%, which is significantly higher than in developed countries such as those in Europe and America; severe pre-eclampsia accounts for approximately 30% to 40% of cases, resulting in a maternal mortality rate as high as 15% to 20% [13]. With the increasing number of older and obese pregnant women, the incidence of pre-eclampsia has been rising year on year, becoming a major public health issue that threatens the health of both mothers and infants [13].

The pathogenesis of pre-eclampsia is related to abnormal placental angiogenesis and endothelial dysfunction, and aspirin can improve placental blood perfusion by inhibiting platelet aggregation and reducing vascular inflammation, thereby reducing the risk of pre-eclampsia. Clinical studies have confirmed that low-dose aspirin (81 $mg \cdot d^{-1}$) taken from the 12th to 28th week of pregnancy can reduce the incidence of pre-eclampsia in high-risk pregnant women by about 30% [13]. The combination of aspirin and low-molecular-weight heparin is more effective in controlling blood pressure levels in high-risk pregnant women and reducing mean arterial pressure, and is the first-line preventive regimen for high-risk pre-eclampsia [13].

3) Treatment of Kawasaki disease in children

Currently, aspirin is the first-line drug for the treatment of cutaneous, mucosal and lymph node syndrome (Kawasaki disease) in children, a systemic vasculitis that mainly affects children under 5 years old and is the leading cause of acquired heart disease in children in many countries [14]. Extensive clinical data indicate that aspirin can effectively alleviate clinical symptoms in children with Kawasaki disease and prevent coronary artery lesions, and it is the cornerstone medication in the treatment of this disease [14]. Its therapeutic effect is achieved through a dual mechanism of anti-inflammatory and antiplatelet aggregation effects, which work synergistically to reduce damage during the acute phase of the disease and long-term cardiovascular risk [14].

Potent anti-inflammatory action to control acute systemic vasculitis: The essence of Kawasaki disease is systemic non-specific vasculitis involving small, medium and large blood vessels [14]. Aspirin attenuates the systemic inflammatory response by inhibiting cyclooxygenase activity in the body, thereby reducing the biosynthesis of inflammatory mediators such as prostaglandins. This action rapidly alleviates acute-phase symptoms such as persistent fever, rash, mucosal congestion and cervical lymph node enlargement, whilst simultaneously mitigating inflammatory damage to the vascular walls, providing crucial support for halting disease progression. In clinical practice, high-dose aspirin (30–50 $mg \cdot kg^{-1} \cdot d^{-1}$) is required during the acute phase to maximize the anti-inflammatory effect, which constitutes the core rationale for its use in Kawasaki disease, distinguishing it from other indications [14].

Inhibition of platelet aggregation and prevention of cardiovascular complications: During the subacute and chronic phases of Kawasaki disease, children exhibit significantly elevated platelet counts, making them prone to platelet aggregation on damaged blood vessel walls, leading to thrombus formation. This is particularly likely to result in coronary artery stenosis, occlusion or aneurysm formation, which is the most serious complication of Kawasaki disease. Aspirin specifically inhibits platelet cyclooxygenase, reducing prostaglandin production, thereby potently inhibiting platelet aggregation and lowering the risk of thrombus formation. In this phase, the dosage of aspirin is reduced to low-dose (3–5 $mg \cdot kg^{-1} \cdot d^{-1}$) for long-term maintenance treatment until the coronary artery lesions recover. This effect persists throughout the course of treatment and is a key mechanism for protecting the coronary arteries and improving long-term prognosis [14].

IV. Adverse Reaction to Aspirin

A. Gastrointestinal and Bleeding Reactions

Gastrointestinal irritation is the most common adverse reaction of aspirin, which is related to its direct irritation of the gastric mucosal barrier and the inhibition of prostaglandin synthesis in the gastric mucosa [2]. Prostaglandins play an important role in protecting the gastric mucosa, such as promoting the secretion of gastric mucus and bicarbonate, and increasing gastric mucosal blood flow [8]. Aspirin inhibits the synthesis of prostaglandins by inactivating COX-1 in gastric mucosal cells, destroying the gastric mucosal protective barrier, and thus causing gastrointestinal discomfort [4]. Oral aspirin may cause upper abdominal discomfort, nausea and other symptoms, and long-term or high-dose use can lead to mucosal erosion, peptic ulcer or even gastrointestinal bleeding [11].

In addition, the antiplatelet effect of aspirin can increase the overall bleeding risk of the body [6]. In addition to gastrointestinal bleeding, common bleeding adverse reactions include nosebleeds, bleeding gums, skin ecchymosis and hematuria [2]. Severe bleeding such as intracranial haemorrhage is rare but life-threatening, especially in patients with uncontrolled hypertension or a history of cerebrovascular disease [9]. Clinically, some patients do not experience effective inhibition of platelet activity following routine aspirin administration, a condition known as ‘aspirin resistance’ [15]. Patients with aspirin resistance not only lose the antiplatelet protective effect but also may have an increased risk of bleeding, which is a major challenge in clinical application [15].

B. Children’s Reactions

Children are a special population for aspirin use, and they have a higher risk of developing allergic reactions following the use of aspirin. A small number of paediatric patients have experienced symptoms such as rash, urticaria, asthma, angioedema or mucosal congestion after taking the medication, with severe cases potentially leading to anaphylactic shock [14]. Attention should be paid to the cross-allergy between aspirin and non-steroidal anti-inflammatory drugs, and aspirin should be avoided in children with a history of allergic rhinitis or asthma [14]. Children are also prone to gastrointestinal reactions after taking aspirin, and gastrointestinal bleeding is a serious adverse reaction in children receiving high-dose aspirin for Kawasaki disease [14]. The pathogenesis is associated with aspirin inhibiting gastric mucosal cell COX-1, reducing protective prostaglandin production and directly irritating the gastric mucosa [14]. Long-term high-dose aspirin for Kawasaki disease may also cause salicylate reaction, with symptoms like headache, dizziness, tinnitus and visual and auditory impairment [14]; the hearing loss caused is usually reversible after drug withdrawal. Reye’s syndrome is a rare but severe adverse reaction in children taking aspirin during viral infections, so aspirin is prohibited for children under 12 years old with viral infections in most countries, and paracetamol is the first choice for antipyretic and analgesic [14].

C. Other Adverse Reactions

In addition to the above adverse reactions, aspirin can also cause other rare adverse reactions, such as liver and kidney function damage, blood system abnormalities, and tinnitus [2]. Mild elevation of liver enzymes may occur during high-dose aspirin use, which is usually reversible and returns to normal after reducing the dosage or discontinuing the drug [14]. Renal function damage is more common in patients with pre-existing renal insufficiency or long-term high-dose use, and the mechanism is related to the reduction of renal blood flow caused by the inhibition of prostaglandin synthesis [2].

Blood system abnormalities such as thrombocytopenia and agranulocytosis are rare, and most occur in patients with long-term high-dose use [2]. Tinnitus and hearing loss are typical manifestations of salicylate intoxication, which are related to the accumulation of salicylate in the inner ear [14]. In addition, aspirin can also interact with other drugs, such as enhancing the anticoagulant effect of warfarin and heparin, increasing the risk of bleeding; reducing the efficacy of angiotensin-converting enzyme inhibitors and diuretics in the treatment of hypertension [6]. Clinical medication should pay attention to avoiding unreasonable drug combinations.

V. Summary and Outlook

Aspirin is a classic integration of traditional medicine and modern science, evolving from an ancient herbal remedy to a modern molecularly targeted drug [1]. Its clinical applications have expanded to cardiovascular and cerebrovascular disease secondary prevention, cancer prevention and children's Kawasaki disease treatment, retaining an important global clinical position [4]. However, it has limitations such as gastrointestinal irritation, bleeding tendency and aspirin resistance, which affect its efficacy [15].

Currently, there is no unified solution for aspirin resistance [15]. Increasing the dose fails to significantly improve platelet COX-1 inhibition but raises adverse reaction risks [15], so low-dose aspirin (75–100 $mg \cdot kg^{-1} \cdot d^{-1}$) remains the optimal choice for cardiovascular secondary prevention [9]. Combination therapy with clopidogrel or ticagrelor offers more effective antiplatelet effects [15]; the COMMIT study showed 7% reduced 30-day mortality and 9% lower recurrence risk in combination therapy for ST-elevation myocardial infarction [15], but dual antiplatelet therapy increases bleeding risks and clopidogrel efficacy varies individually [15], requiring personalized dosing based on patient condition and platelet function tests [15].

Although aspirin-resistant patients face a 3.5-fold higher cardiovascular death risk [15], aspirin therapy reduces cardiovascular events by 25% for most patients [10], with benefits outweighing risks [9]. Understanding aspirin resistance mechanisms (genetic factors, platelet pathways, drug interactions) helps reduce incidence and enable personalized application [15]. Aspirin resistance has become a major frontier in contemporary pharmaceutical research, connecting this century-old drug to key unresolved challenges in modern clinical pharmacology.

Looking ahead, with the in-depth development of precision medicine and molecular pharmacology, the research on aspirin will continue to advance in depth, and its clinical value will be further unlocked:

Personalized precision medicine: Through technologies such as genetic testing, identifying which patients stand to benefit most from aspirin treatment (maximizing efficacy) and which patients face a higher risk of bleeding (minimizing risk), thereby achieving truly 'tailor-made' medication.

Development of new formulations: Research into safer formulations, such as more advanced enteric-coated tablets and combination preparations (combined with proton pump inhibitors to protect the gastric mucosa), to further improve safety.

Exploration of new indications: Continued in-depth exploration of its preventive and therapeutic roles in diseases such as Alzheimer's disease and other types of cancer, and elucidation of its molecular mechanisms.

Rediscovery of mechanisms of action: Beyond the COX pathway, scientists are also exploring other potential targets for aspirin, such as anti-inflammatory effects via the NF-κB pathway and the induction of cancer cell apoptosis; these studies may offer entirely new perspectives on its applications.

In summary, the story of aspirin is far from over. This 'evergreen' compound, born a century ago, is constantly sprouting new shoots under the light of modern science, continuing to safeguard human health and showcasing the enduring appeal of science and medicine.

Conflict of Interest

The author declares no conflict of interest.

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References

[1] V. Fuster and J. M. Sweeny, "Aspirin: A historical and contemporary therapeutic overview," *Asian J. Pharm. Clin. Res.*, vol. 3, pp. 768–778, 2011.

[2] J. Wick, "Aspirin: A history, a love story," *Consult. Pharm.*, vol. 27, no. 5, pp. 322–329, 2012.

[3] D. Jeffreys, Aspirin: The remarkable story of a wonder drug. Bloomsbury Publishing, 2004.

[4] W. Sneader, "The discovery of aspirin: a reappraisal," *BMJ*, vol. 321, no. 7276, pp. 1591–1594, 2000.

[5] P. C. Elwood, A. L. Cochrane, and M. L. Burr, "A randomized controlled trial of acetylsalicylic acid in the secondary prevention of mortality from myocardial infarction," *Br. Med. J.*, vol. 4, pp. 436–440, 1974.

[6] W. S. Fields, N. A. Lemak, and R. F. Frankowski, "Controlled trial of aspirin in cerebral ischemia," *Stroke*, vol. 8, pp. 301–314, 1977.

[7] G. Starmer and Z. W. Shi, "History of aspirin and its usage mode (Part 1)," *Pharm. Inf. Bull.*, vol. 1, pp. 29–31+28, 1984.

[8] H. J. Lü, B. P. Li, and B. Zhou, "Clinical effect observation of low-dose aspirin combined with Ganshuyu capsule in the treatment of primary dysmenorrhea," *Henan Med. Res.*, vol. 27, pp. 1606–1607, 2018. (in Chinese)

[9] M. Y. Li, W. L. Shi, and H. Y. Duan, "Aspirin for primary prevention of cardiovascular diseases in adults: interpretation of the recommendation statement from the US preventive services

task force," *Chin. J. Gen. Med.*, vol. 27, pp. 1277–1282, 2024. (in Chinese)

[10] J. Q. Zhang, Y. H. Wang, and M. L. Liu, "Research progress of aspirin in secondary prevention of cardiovascular diseases," *Chin. Circ. J.*, vol. 38, pp. 887–890, 2023. (in Chinese)

[11] R. F. Guo, D. Kang, and Z. C. Leng, "Research progress on preventive and therapeutic effects and mechanism of aspirin on gastric cancer," *Shandong Med. J.*, vol. 65, pp. 126–129, 2025. (in Chinese)

[12] T. Tao, P. Xiao, and M. M. Ding, "Research progress and controversy on the application of aspirin in the prevention and treatment of liver cancer," *Chin. J. Clin. Hepatol.*, vol. 36, pp. 1847–1851, 2020. (in Chinese)

[13] Y. Q. Wang, H. Cai, and M. D. Li, "Effectiveness and safety of aspirin in the preeclampsia period: updated systematic review and meta-analysis of dose response," *Chin. J. Hypertens.*, pp. 1–10, 2025. (in Chinese)

[14] Y. Zhu, Z. Z. Li, and H. B. Sun, "Adverse reaction analysis of aspirin in children," *World Clin. Drugs*, vol. 42, pp. 925–930, 2021. (in Chinese)

[15] W. W. Lin, H. Y. Peng, and Y. Liu, "Current status and prospect of aspirin resistance," in *Proc. Guangdong Pharmacist Conf.*, 2016, pp. 1150–1155.