Proceedings of ICMMGH 2026 Symposium: Cell and Molecular Biology: Understanding Immune Cell Functions
DOI: 10.54254/2753-8818/2026.PJ30527

The Pharmacological Mechanism and Clinical Application of Aspirin

Meilun Dai

Guangdong Country Garden School, Foshan, China
daimeilun@gcgsedu.com

Abstract. The history of aspirin development follows a systematic drug research route, starting with the natural medicinal use of willow bark and culminating in the synthesis of acetylsalicylic acid in 1897, leading to a theoretical understanding of its action in blocking cyclooxygenase (COX) by 1971. The majority of its mechanisms are blocking the synthesis of prostaglandins by permanently acetylating the serine residues of COX-1/COX-2. It also prevents the platelet aggregation even in low doses. Clinically, it is frequently employed due to its effective use as an agent against mild/moderate inflammation, moderate pain, and fever; cardiovascular and cerebrovascular diseases; the risk of colorectal and gastric cancer; and Alzheimer's disease. Some of the safety risks are gastrointestinal damage, asthma caused by the use of aspirin, and hemorrhage during pregnancy. Choose enteric-coated preparations first, monitor the delivery of low-dose preparations, screen high-risk groups, and conduct clinical screening. In the future, having incorporated precision medicine, targeted delivery, and artificial intelligence technologies, aspirin has the potential to undergo personalization in both the prevention and treatment of tumors and neurodegenerative diseases, so its clinical potential continues to grow.

Keywords: Aspirin, Pharmacological mechanism, Clinical application, Non-steroidal anti-inflammatory drugs, New uses of old medicine

1. Introduction

The history of the development of aspirin is over three thousand years and the medicine is already considered one of the most popular classic medicines in the world. It represents the scientific rationale of natural product formation and therapeutic investigation, from the primeval willow-bark medicine all the way to today's chemical synthesis and elucidation of the mechanism. Since the isolation of salicin and the structural optimization of acetylsalicylic acid itself up to the discovery of its pharmacological actions and growth of its clinical use, the development of aspirin has paralleled both medical and chemical progress. A literature review of its history of development enriches our comprehension of non-steroidal anti-inflammatory drugs (NSAIDs) and also offers a time-honored example of the translation of natural products into clinical drugs. It also provides practical information that can be used in the prevention and treatment of cardiovascular and cerebrovascular diseases, inflammatory conditions, etc. At the same time, it offers important hints to drug development via the use of repurposing old drugs and community health control. This paper will

© 2026 The Authors. This is an open access article distributed under the terms of the Creative Commons Attribution License 4.0 (https://creativecommons.org/licenses/by/4.0/).

DOI: 10.54254/2753-8818/2026.PJ30527

discuss the scientific background and medical importance of aspirin, a miracle drug of the century, by exploring four broad levels: history, pharmacological actions, clinical uses, and constraints/safety. It stresses its continuous contribution to world health and medical advances.

2. Tracing historical source

People knew the analgesic and antipyretic action of the willow bark as early as the Sumerian and Egyptian civilizations. Hippocrates, the father of Greek medicine, did use the willow leaf decoctions to treat work pains and fever. Salicin was indicated to be its active ingredient. Organic chemistry in the 19th century assisted researchers in extracting salicin out of willow bark and degrading it to salicylic acid. Salicylic acid was corroborated to have antipyretic, analgesic, and anti-inflammatory effects. It was rarely used because of its excessive gastrointestinal effects and foul taste. Even though the knowledge is preliminary, this research defined the pharmacological action and major undesirable side effects. To enhance salicylic acid, in 1897 Cornelius Bayer AG chemist Felix Hoffmann synthesized acetylsalicylic acid by the acetylation of salicylic acid to increase its solubility. This chemical modification spared the irritation of the stomach mucosa of salicylic acid and retained its pharmacological activity. Bayer produced this chemical in the year 1899 under the name Aspirin. An example of a classic unnecessary optimization of structure is salicylic acid to acetylsalicylic acid, which optimized medication safety and acceptability on the basis of preclinical trials.

3. Pharmacological mechanism

Currently, the pharmacological properties of aspirin majorly include anti-inflammatory, analgesic, and antipyretic activity.

The release of prostaglandins (mainly PGE 2 and PGF) and constrictor substances in rabbit aorta (RCS) was first discovered in 1969 by Piper and Vane at the conclusion of lung perfusion experiments using sensitized guinea pigs. Aspirin potently suppressed both substances and inhibited tissue contraction through the effects of prostaglandins. After this finding, Vane proposed that this specific process was the primary effect of aspirin, which is the inhibition of prostaglandin synthesis. Incubation of arachidonic acid in the presence of aspirin with the guinea pig lung cell homogenate supernatant suppressed dose-dependently PGF2 synthesis, which was deemed by Vane using experimental results. It appeared in Nature in 1971, and parallel experiments demonstrated that orally administered aspirin had decreased the amounts of prostaglandins released by human platelets, canine spleen, and human semen. These studies in other species, other organs, and other dosage modalities established that aspirin inhibits production of prostaglandin. This reaction is a widely used mechanism that makes it anti-inflammatory, analgesic, and antipyretic.

The successful isolation and identification of cyclooxygenase (COX/PGHS) was done in 1976. It is an endosomal-membrane protein located in the endoplasmic reticulum and can catalyze the conversion of arachidonic acid (an unsaturated fatty acid, the basic component of prostaglandin production) into prostaglandins (which is based on the synthesis of PGG 2, which is then reduced to PGH 2). This enzyme exhibits both cyclooxygenase and peroxidase activities. Aspirin permanently inhibits the production of prostaglandins as it acetylates the active site, the serine residue of the enzyme (Ser530). Repair entails the production of enzymes. Aspirin quickly, and specifically, acetylates this enzyme at low levels and non-selectively acetylates a myriad of biomolecules at high levels. At the sites of inflammation, prostaglandins are increased. Redness, heat, and swelling are brought about by vasodilation and vascular permeability. Moreover, it invites inflammatory cells,

DOI: 10.54254/2753-8818/2026.PJ30527

which raises the infiltration. Aspirin inhibits the production of prostaglandins, thereby reducing pro-inflammatory effects. Prostaglandins reduce the pain threshold of the peripheral receptors and raise the sensitivity of the stimuli. They also increase the pain attachments of the central nervous system. Inhibition of the production of prostaglandins reduces the sensitivity of receptors and amplification of pain, inhibiting pain. Prostaglandins, and particularly PGE_2, mediate the occurrence of the antipyretic effect by influencing the hypothalamus thermoregulatory center and increasing the body thermostat. This process leads to fever through an augmented production of heat and a reduced heat loss. Aspirin inhibits central production of prostaglandins, which decreases the thermostat set point and inhibits fever [1,2].

4. Clinical application

4.1. Anti-inflammatory

A team of Japanese scientists studied animals by using rats and guinea pigs as experimental subjects in order to put up distinct experimental models. Aspirin dose-dependently inhibited and had high efficacy against carrageenan-induced paw oedema, cotton ball granuloma formation, and adjuvant-induced arthritis in rats (ED 50: 143.6 mg/kg). Aspirin demonstrated great effects of inhibition against guinea pig ultraviolet erythema (75.6% inhibition rate at 80 mg/kg) and even in arachidonic acid-induced skin erythema (inhibition rate about 50% at 100 mg/kg) [3].

Moreover, sleep deprivation can also be one of the close factors with inflammation. It is a randomized, double-blind, crossover trial that was carried out by a research team from Harvard Medical School with 46 participants. The three groups were sleep-deprived + low-dose aspirin (39 participants, who slept only 4 hours per night throughout the course of 5 days, taking 81 mg aspirin per day), sleep-deprived + placebo (37 participants), and regular sleep + placebo (37 participants). The findings proved that in comparison to the sleep-deprived + placebo group, the aspirin users had much lower levels of interleukin-6 (IL-6), much lower levels of C-reactive protein (CRP), and a lower percentage of cyclooxygenase (COX)-1/COX-2 double-positive monocytes. These results totally reflect the inhibitory nature of aspirin on sleep deprivation-induced inflammation [4].

4.2. Analgesia

Aspirin applies effectively to mild to moderate inflammatory pains like headaches, toothaches, muscle pain, and joint pain. A Cochrane comprehensiveness review regarding early postpartum perineal discomfort was an episiotomy-associated pain study comprising 1132 non-breastfeeding women in 17 RCTs published in the years 1967 to 1997. There was a pain evaluation (4 to 8 hours after administration of a drug) based on patient-reported adequate rate of pain relief and two measures of pain assessment, SPID and TOTPAR. Aspirin (300 mg to 1200 mg) as a single dosage was also of significance to reduce the perineal pain, with 25.3 and 51.3 as the placebo and aspirin numbers, respectively, with the risk ratio (RR) of 2.03 with a confidence interval (95) of 1.69 to 2.42 [5]. A virtual study of 2.294 million US adults aged 40 years and above with significant chest pain considered the time point of intervention as within 4 hours of chest pain onset. These findings indicated that self-prescription of 325 mg aspirin was an effective way of reducing the risk of AMI-related mortality, postponing 13 016 AMI mortality, and preventing 166 309 life years. The saving to a life year cost was US $3.70, and the mortality of AMI reduction was greater than ten times the risk of bleeding. This report confirms that aspirin self-management reduces significantly AMI mortality,

DOI: 10.54254/2753-8818/2026.PJ30527

overriding the bleeding risks. It is an incredibly cost-efficient intervention that is not limited by the healthcare resources and personal socioeconomic status [6].

4.3. Antipyretic

A group of scientists from Europe were able to conduct a clinical study to examine the relationship between aspirin dosage and the effect of aspirin in preventing the symptoms of fever in pediatric patients. There were 145 children (3 months to 11.5 years) with a 38.9°C baseline rectal temperature who took part in the study. The use of other antipyretics in the previous 24 hours was avoided. The participants were placed randomly into the 5 mg/kg, 10 mg/kg, and 15 mg/kg aspirin groups. The rectal temperature was recorded at 30 minutes of the treatment and hourly up to 6 hours after the administration. Clinically effective was the reduction of temperature to less than 38.9°C. Both dosages have produced significant temperature reduction at any point of 1-6 hours of administration. The antipyretic activity of the 10 mg/kg, as well as the 15 mg/kg group, was found to have a significantly stronger effect compared to that of the 5 mg/kg group ($P < 0.05$) [7].

4.4. Other clinical application

Aspirin irreversibly and permanently blocks platelet COX-1, which prevents platelet aggregation, the synthesis of TXA2, and thrombosis [8]. Platelets have no nucleus, and they are unable to resynthesize COX. Taking low doses of aspirin on a long-term basis can possibly lower the risk of colorectal cancer by suppressing inflammation of the mucous membranes and cell proliferation through the action of the COX-2 enzyme [9]. It also prevents stomach cancer. Aspirin used as a low dose and taken over a long period of time considerably lowers the risk of stomach cancer. This procedure is done by COX-dependent pathways (reducing the production of prostaglandin, inhibiting angiogenesis, and inhibiting platelet aggregation) and non-COX-dependent pathways (controlling the expression of oncogene and tumor suppressor genes) [10]. It has been proposed by research that the incidence of Alzheimer's disease can be reduced by aspirin in the long term in the old population. This advantage could be attributed to the fact that it enhances microcirculation and decreases neuroinflammation via acetylation of protein targets and, consequently, slows cognitive impairment [11,12].

5. Limitation and safety

Inasmuch as aspirin is a wonderful drug, it has some limitations. The most common side effect of aspirin is gastrointestinal damage. It can either directly induce irritation of the stomach mucosa or inhibit gastric COX-1, leading to reduced production of PGE2 and PGI2. They include enhanced acidic levels in the stomach, reduced levels of mucus and bicarbonate, and reduced blood flow of the mucosa. These lesions render mucosa susceptible to erosion, ulceration, and hemorrhage or perforation [13]. Patients should use enteric-coated aspirin to minimize stomach dissolution and mucosal injury. Make sure the treatment works; it is preferable to small-dose treatment, and it is not taken over a long period of time. Gastrointestinal function in long-term therapy should be checked in patients. It is possible that since leukotriene production increases, a few patients can have allergic reactions of urticaria, angioedema, or asthma attacks caused by aspirin [14]. Therefore, the screening of asthma and allergy history of high-risk people at the pre-treatment stage is needed. At-risk patients in case of aspirin-induced asthma ought to not take the drug or undergo a closely monitored desensitization to the drug. Aspirin, when given in low doses, can augment postpartum

DOI: 10.54254/2753-8818/2026.PJ30527

blood loss and hemorrhage [15]. It should exclusively be used by high-risk pregnant women whose condition is pre-eclampsia or placental abruption. It is not to be used blindly on healthy pregnant women. The users would need to employ and have extensive risk management during the treatment process and have close postnatal observation of bleeding and, where necessary, take immediate action.

6. Conclusion

The history of aspirin as a curative drug in both antiquity and the contemporary anti-inflammatory/analgesia/antipyretic uses demonstrates the fundamental worth of drug research. It was on this trip that the scope of medicinal applications of aspirin was seen, and its significant safety issues were noted (such as gastrointestinal injury and bleeding). The preclinical research systems that are fulfilled in contemporary drug development are far more intricate and controlled than during the time of aspirin, although its case study cautions those working in it that profound examination of drug-body association leads to pharmaceutical progress and safe and effective medication. Its success will continue to inform the development of drugs. Individualized aspirin treatment can lower the risks of gastrointestinal damage through future precision medicine and genetic testing that can identify a personalized aspirin dose based on the population and dose. Specific methods of delivery and detection technologies that use nanotechnology will be invented, and researchers will consider its application in cancer prevention and neurological diseases. Through the assistance of artificial intelligence and big data, further clarification of its action mechanisms will allow this traditional drug to reinvent its purpose in modern-day medicine, thus protecting human health more effectively.

References

[1] Desborough MJR, Keeling DM. The aspirin story - from willow to wonder drug. Br J Haematol. 2017 Jun; 177(5): 674-683.
[2] Vane JR, Botting RM. The mechanism of action of aspirin. Thromb Res. 2003 Jun 15; 110(5-6): 255-8.
[3] Spirin and Salicylicacid antiinflammatory and tingalgic. Foliapharmacol.japon.85, 49-57(1985).
[4] Engert LC, Ledderose C, Biniamin C, Birriel P, Buraks O, Chatterton B, Dang R, Daniel S, Eske A, Reed T, Tang A, Bertisch SM, Mullington JM, Junger WG, Haack M. Effects of low-dose acetylsalicylic acid on the inflammatory response to experimental sleep restriction in healthy humans. Brain Behav Immun. 2024 Oct; 121: 142-154.
[5] Shepherd E, Grivell RM. Aspirin (single dose) for perineal pain in the early postpartum period. Cochrane Database Syst Rev. 2020 Jul 24; 7(7): CD012129.
[6] Russo RG, Wikler D, Rahimi K, Danaei G. Self-Administration of Aspirin After Chest Pain for the Prevention of Premature Cardiovascular Mortality in the United States: A Population-Based Analysis. J Am Heart Assoc. 2024 Jun 4; 13(11): e032778.
[7] Vigano A, Dalla Villa A, Cecchini I, Biasini GC, Principi N. Correlation between dosage and antipyretic effect of aspirin in children. Eur J Clin Pharmacol. 1986; 31(3): 359-61.
[8] Fuster V, Sweeny JM. Aspirin: a historical and contemporary therapeutic overview. Circulation. 2011 Feb 22; 123(7): 768-78.
[9] Drew DA, Cao Y, Chan AT. Aspirin and colorectal cancer: the promise of precision chemoprevention. Nat Rev Cancer. 2016 Mar; 16(3): 173-86.
[10] Guo Ruifang, Kang Dong, Ye Zhengcai, et al. Research Progress on the preventive and Therapeutic effects and Mechanisms of Aspirin on Gastric cancer [J]. Shandong Medicine, 2020, 65(8): 126-129.
[11] Zhou Borong, Xu Zhiqiang, Kuang Yongfeng, et al. Study on the Efficacy of Enteric-coated Aspirin in Delaying the Progression of Alzheimer's Disease [J]. Chinese Journal of Clinical Rehabilitation, 2004, 8(16): 3020-3021.
[12] Ayyadevara S, Balasubramaniam M, Kakraba S, Alla R, Mehta JL, Shmookler Reis RJ. Aspirin-Mediated Acetylation Protects Against Multiple Neurodegenerative Pathologies by Impeding Protein Aggregation. Antioxid

DOI: 10.54254/2753-8818/2026.PJ30527

Redox Signal. 2017 Dec 10; 27(17): 1383-1396.
[13] Ivey KJ. Gastrointestinal effects of antipyretic analgesics. Am J Med. 1983 Nov 14; 75(5A): 53-64.
[14] Sanak M. Aspirin induced asthma: a still evolving area of basic and clinical research. Pol Arch Intern Med. 2022 Feb 28; 132(2): 16219.
[15] Jiang Y, Chen Z, Chen Y, Wei L, Gao P, Zhang J, Zhou X, Zhu S, Zhang H, Du Y, Fang C, Su R, Wang S, Yu J, He M, Ding W, Feng L. Low-dose asprin use during pregnancy may be a potential risk for postpartum hemorrhage and increased blood loss: a systematic review and meta-analysis. Am J Obstet Gynecol MFM. 2023 Apr; 5(4): 100878.