Volume 3, Issue 2, February 2025 ISSN (E): 2938-3765

SALICYLATES ARE ANTI-INFLAMMATORY DRUGS AND THEIR ACTION MECHANISM

Nafisaxon Xasanboyeva Abdullajonovna
Assistant of the Department of Pharmacology of Fergana
Medical Institute of Public Health

Abstract
Nonsteroidal anti-inflammatory drugs are aspirin-type or non-narcotic or non-opioid analgesics. In addition, they have anti-inflammatory, antipyretic and uricosuric properties— without addiction liability. They act by inhibiting prostaglandin synthesis. NSAIDs (nonsteroidal anti-inflammatory drugs) can reduce pain, fever and other types of inflammation.

Keywords: Effect, treatment, mechanism, aspirin, inhibitor, chemical, pain.

Introduction

The medicinal effects of the bark of the willow tree have been known since centuries. The active principle 'salicin' was isolated from the willow bark. This salicin is converted to glucose and salicylic acid in the body. In 1875, sodium salicylate was first used in the treatment of rheumatic fever. After its anti-inflammatory and uricosuric properties were established, efforts were made to synthesize derivatives which were less expensive and aspirin was introduced in 1899. Now the synthetic compounds have replaced the natural ones in the market.

Mechanism of Action of NSAIDs: During inflammation, arachidonic acid liberated from membrane phospholipids is converted to prostaglandins (PGs), catalyzed by the enzyme cyclo-oxygenase (COX). These prostaglandins produce hyperalgesia—they sensitize the nerve endings to pain caused by other mediators of inflammation like bradykinin and histamine. NSAIDs inhibit the PG synthesis by inhibiting the enzyme cyclo-oxygenase and is the major mechanism responsible for pharmacological effects of aspirin. Aspirin is an irreversible inhibitor of COX (acetylates COX) while the others are reversible competitive COX inhibitors. There are two forms of cyclo-oxygenase, viz. COX-1 is found in most of the normal cells (constitutive) and is involved in maintaining tissue homeostasis. COX-2 is induced in the inflammatory cells by cytokines and other mediators of inflammation. This COX-2 catalyzes the synthesis of prostanoids which are the mediators of inflammation. Most NSAIDs inhibit both COX-1 and COX-2 while some newer agents like celecoxib and rofecoxib selectively inhibit only COX-2.

Salicylates are salts of salicylic acid, e.g. methyl salicylate, sodium salicylate, acetylsalicylic acid (aspirin). Aspirin is taken as the prototype.

Analgesia: Aspirin is a good analgesic and relieves pain of inflammatory origin. This is because PGs are formed during inflammation and they sensitize the tissues to pain and aspirin inhibits PG synthesis. Pain originating from the integumental structures like muscles, bones, joints, and pain in connective tissues is relieved. But in vague visceral pain, aspirin is relatively ineffective. The pain is relieved without euphoria and hypnosis. Hence there is no development of tolerance and

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dependence. But aspirin is a weaker analgesic when compared to morphine. Antipyretic action: In presence of fever, salicylates bring down the temperature to normal level. But, in normal individuals, there is no change in temperature. In fever, pyrogen, a protein, circulates in the body and this increases the synthesis of PGs in the hypothalamus, thereby raising its temperature set point. The thermostatic mechanism in the hypothalamus is thus disturbed. Aspirin inhibits PG synthesis in the hypothalamus and resets the thermostat at the normal level bringing down the temperature. Enhanced sweating and cutaneous vasodilatation promote heat loss and assist in the antipyretic action. Anti-inflammatory action: At higher doses of 4–6 g/day, aspirin acts as an antiinflammatory agent. Signs of inflammation like tenderness, swelling, erythema and pain are all reduced or suppressed. But, the progression of the disease in rheumatoid arthritis, rheumatic fever or osteoarthritis is not affected. Once again the mechanism involved is PG synthesis inhibition—PGs present in inflammatory tissues are responsible for edema, erythema and pain. In addition, aspirin also interferes with the formation of chemical mediators of the kallikrein system. As a result, it decreases the adherence of granulocytes to the damaged vasculature, stabilizes lysosomes and decreas.

Respiration: In therapeutic doses of 4–6 g/day, salicylates increase consumption of oxygen by skeletal muscles. As a result, there is increased CO2 production. This increased CO2 stimulates the respiratory centre. Salicylates also directly stimulate the medullary respiratory centre. Both these actions increase the rate and depth of respiration. These effects are dose-dependent. es the migration of the polymorphonuclear leukocytes and macrophages into the site of inflammation. As a result of this stimulation of respiration, plasma CO2 is washed out leading to respiratory alkalosis. With toxic doses, the respiratory centre is depressed leading to respiratory failure. Acid–base and electrolyte balance: In antiinflammatory doses, salicylates produce significant respiratory stimulation—more CO2 is washed out resulting in respiratory alkalosis; pH becomes alkaline. This is compensated by increased excretion of HCO3 – in the urine accompanied by Na+, K+ and water. pH then returns to normal. This stage is known as compensated respiratory alkalosis. With toxic doses, salicylates depress the respiratory centre directly. As a result, CO2 accumulates because more CO2 is produced than is exhaled. Thus plasma CO2 rises and pH decreases. Since the concentration of HCO3 – is already low due to enhanced renal excretion, the change results in uncompensated respiratory acidosis. This is superimposed by metabolic acidosis caused by accumulation of acids. Toxic doses also depress vasomotor centre. This vasomotor depression impairs renal function resulting in accumulation of strong acids of metabolic origin like lactic, pyruvic and acetoacetic acids. The above effects are accompanied by dehydration due to: water lost in urine with $HCO3^-$, Na+ and K+, Increased sweating, water lost during hyperventilation. Thus there is severe dehydration with acidosis.

Metabolic effects: Salicylates enhance the cellular metabolism due to uncoupling of oxidative phosphorylation. More of O2 is used and more CO2 is produced, especially in skeletal muscles, leading to increased heat production. In toxic doses, hyperpyrexia, increased protein catabolism with resultant amino- aciduria and negative nitrogen balance are seen. Enhanced utilization of glucose leads to mild hypoglycemia. But in toxic doses, hyperglycemia occurs due to central sympathetic stimulation which increases adrenaline levels.

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Gastrointestinal tract: Aspirin is a gastric irritant. Irritation of the gastric mucosa leads to epigastric distress, nausea and vomiting. Aspirin also stimulates the CTZ to produce vomiting. Erosive gastritis, mucosal congestion, gastric ulceration and GI bleeding resulting in malaena and occasionally haematemesis can occur particularly in higher doses.

Mechanism: In the acidic pH of the stomach, salicylates remain unionised. These drug particles adhere to the mucosa producing irritation. These particles also diffuse into the gastric mucosal cells. Inside the cells, as the pH is alkaline, the drug particles get ionised and the ions cannot move back into the lumen ion trapping—resulting in more toxicity. The ions promote local back diffusion of acid.

PGs are cytoprotective to gastric mucosa because they reduce acid secretion, increase mucus production and mucosal blood flow. As aspirin inhibits synthesis (irreversible inhibitor of COX), the defence mechanism of PGs is lost. iv. Antiplatelet effect of aspirin may result in increased bleeding if there is any gastric erosion. The above actions make aspirin ulcerogenic. With soluble aspirin, gastric irritation is less. The selective COX-2 inhibitors cause less gastric irritation because gastric epithelial cells have COX-1.

Immunological effects: In higher doses, salicylates suppress several antigen– antibody reactions including inhibition of antibody production, Ag–Ab aggregation and antigen-induced release of histamine. These effects might also contribute to the beneficial effects in rheumatic fever. Uric acid excretion: Uric acid is excreted by secretion from the distal tubules. In a dose of 1–2 g/day, aspirin increases plasma urate levels by urate retention because it interferes with urate secretion by the distal tubules. Large doses of >5 g/day increase urate excretion because it inhibits reabsorption of urate by proximal tubule causing uricosuria. But, its uricosuric effect cannot be used therapeutically because high doses are required and such doses result in prominent adverse effects. Blood: Even in small doses, aspirin irreversibly inhibits platelet cyclo-oxygenase (acetylates COX) and thereby TXA2 synthesis by the platelets. It, therefore, interferes with platelet aggregation and prolongs the bleeding time. Even a single dose can irreversibly inhibit TXA2 synthesis which is for the life of the platelets (8–11 days). Platelets contain only COX-1. Fresh platelets have to be formed to restore TXA2 activity, because platelets cannot synthesize proteins as they have no nuclei— which means, COX cannot be regenerated. Moreover, aspirin inhibits platelet COX in the portal circulation itself and, therefore, even small doses (40 mg daily) of aspirin is adequate for its antiplatelet aggregatory effects. Other NSAIDs are reversible inhibitors of platelet cyclo-oxygenase. Local effects:

Salicylic acid when applied locally is a keratolytic. It also has mild anti-septic and fungistatic properties. Salicylic acid is also an irritant for the broken skin.

References

1. Khasanboeva, N. A. (2023). VITAMIN B12 DEFICIENCY AND DRUGS USED IN ITS TREATMENT. SO ‘NGI ILMIY TADQIQOTLAR NAZARIYASI, 6(10), 52-59.
2. Khasanboeva, N. A. (2023). Fees in Folk and Modern Medicine. The Peerian Journal, 14, 14-17.

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

3. Khasanboeva, N. A. (2023). MEDICINAL PLANTS OF THE FERGANA REGION. International Journal of Medical Sciences And Clinical Research, 3(02), 1-4.
4. Хасанбоева, Н. А. (2021). ЦЕЛЕБНЫЕ СВОЙСТВА ПРЕПАРАТОВ, ПОЛУЧЕННЫЕ ИЗ ПРОДУКТА ХВОИ. Интернаука, 22, 76.
5. Abdullajonovna, H. N. INTERACTION BETWEEN DRUG SUBSTANCES AND NUTRIENT PRODUCTS. International Journal of Advanced Research in ISSN, 2278-6252.
6. Abdullojonovna, K. N. (2021). In the Chronopharmacology of Drugs and Medicinal Substances. Academicia Globe, 2(6), 225-228.
7. Khasanboeva, N. A. (2023). VITAMIN B12 DEFICIENCY AND DRUGS USED IN ITS TREATMENT. SO 'NGI ILMIY TADQIQOTLAR NAZARIYASI, 6(10), 52-59.
8. Абдуллажоновна, НХ (2025, февраль). ПОБОЧНЫЕ ЭФФЕКТЫ САЛИЦИЛАТОВ. На Международной конференции педагогов (стр. 119-125).
9. Zakhriddinovich, I. B., & Ilhomjon Ma'mur o'g, Q. (2025, January). HYPERNATREMIA IN CHILDREN AND NEUROLOGICAL DISORDERS, ITS MANAGEMENT. In International Conference on Multidisciplinary Sciences and Educational Practices (pp. 70-76).
10. Pattoyevich, G. A., & Nilufar, M. (2025, January). CHILDREN'S ECZEMA AND RECOMMENDATIONS FOR ITS TREATMENT. In International Conference on Multidisciplinary Sciences and Educational Practices (pp. 56-62).
11. Pattoyevich, G. A. (2025, February). PRIMARY INSTRUMENTAL EXAMINATION IN THE ANOMALY OF PULMONARY ATRESIA WITH INTACT VENTRICULAR SEPTUM. In International Educators Conference (pp. 148-154).
12. Шухратжон у'г'ли, СЭ (2025, январь). РАСПРОСТРАНЕННОСТЬ И ЭТИОЛОГИЯ ГИПОСПАДИИ. На Международной конференции по междисциплинарным наукам и образовательной практике (стр. 99-104).
13. Melibayevna, B. X. (2025, February). EXTERNAL OTITIS IN CHILDREN AND ITS TREATMENT. In International Educators Conference (pp. 133-139).
14. Umarovich, B. M., & Bahodir o'g'li, U. B. (2025, February). CLINICAL AND LABORATORY CHARACTERISTICS OF CHRONIC VIRAL HEPATITIS" B" AND" C" IN HIV-INFECTED INDIVIDUALS. In International Educators Conference (pp. 144-147).
15. Qodirova, G. A., & Ibrohimova, M. (2025, February). TREATMENT METHODS AND COMPLICATIONS OF SCARLET FEVER. In International Educators Conference (pp. 175-181).
16. Абдукадирова, Д. Т., Абдукадиров, У., & Жабборов, А. (2022). ДИАБЕТИЧЕСКАЯ ПОЛИНЕЙРОПАТИЯ: ПУТИ ПОЛНОЦЕННОЙ КОРРЕКЦИИ НЕВРОЛОГИЧЕСКОГО ДЕФИЦИТА. Journal of new century innovations, 18(3), 316-319.
17. ANVAROVA, Z. (2024). TIBBIYOTDA BOLALAR BO 'G 'IMLARINING ANATOMIK VA FUNKSIONAL XUSUSIYATLARI ETIOLOGIYASI VA PATOGENEZINI O 'QITISHDA PEDAGOGIK YONDASHUV KLINIKASI VA TASNIFI. News of the NUUz, 1(1.9), 50-53.

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