

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Pharmaceutical Sciences

Review Article.....!!!

Received: 12-03-2020; Revised: 30-03-2020; Accepted: 02-04-2020

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) EDIBLE VACCINE: A REVIEW

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Keywords:

Non-Steroidal Anti-
Inflammatory Drugs, Aspirin ,
Celecoxib

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ABSTRACT

Non-Steroidal anti-inflammatory drugs (NSAIDs) are largely used for treatment of acute and chronic pain as well as inflammation, even for long periods of time (months or years). NSAIDs include the nonselective or traditional NSAIDs, as well as the cyclo-oxygenase-2 specific ones. The nonselective or traditional agents are still widely used, and are also freely available as over the-counter analgesics. However, NSAIDs are known for multiple adverse effects, including gastrointestinal bleeding, cardiovascular side effects, and NSAIDs induces nephrotoxicity. Due to their anti-inflammatory properties, these drugs have been investigated for their anticancer effects in numerous studies

INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) are used worldwide to treat pain and inflammation (1). Among world's population over 30 million people utilize non-steroidal anti-inflammatory drugs for treatment of their discomfort. Approximately half these patients are over the age of 65 years and use NSAIDs on daily basis (2). They are often used to relieve symptoms of Headache, painful periods, sprains and strains, cold and flu, arthritis and other causes of long term pain. Although NSAIDs are commonly used, they are not suitable for everyone and can sometimes cause troublesome side effects (3). NSAIDs are associated with a small increase in the risk of a experiencing a heart attack, stroke, or heart failure. These risks are related to how long they are used for, the dosage and certain types of NSAIDs (4). Non-steroidal anti-inflammatory drugs (NSAIDs) alleviate pain by counteracting the Cyclooxygenase (COX) enzyme, on its own, COX enzyme synthesizes prostaglandins, creating inflammation. In whole, the NSAIDs prevent the prostaglandins from ever being synthesized, reducing or eliminate the pain (5). During therapy with NSAIDs, the patient is at risk of gastrointestinal and renal toxicity, which have long been known. Increase in arterial blood pressure (BP) during the administration of NSAIDs and the risk of heart failure exacerbation were also described decades ago (6). NSAIDs act by inhibiting cyclooxygenase-1 (COX-1) and COX-2 enzymes, which are involved in prostaglandin synthesis, resulting in their analgesic, anti-inflammatory, and antipyretic effect (7). All NSAIDs are available on prescription, while some are also available in lower dose over-the-counter forms that can be obtained without a prescription (8). One of the mechanisms which have been associated with the adverse effects of NSAIDs is the generation of oxidative stress (9). NSAIDs are a heterogeneous group of non-opioid analgesics and anti-inflammatory agents (10). NSAIDs are effective analgesic and anti-inflammatory drug that form the main pharmacological approach to treating various forms of pain, and particularly chronic musculoskeletal pain, but have a number of known adverse effects. NSAIDs (and aspirin) are associated with upper and lower gastrointestinal harm, acute renal failure and congestive heart failure (11). Non-steroidal anti-inflammatory drugs (NSAIDs) are the most frequently prescribed medication worldwide and are commonly used for treating low-back pain (12). NSAIDs work by slowing the formation of compound known as prostaglandins. Prostaglandins play an important role in the body's inflammatory response. NSAIDs block an enzyme called cyclooxygenase, also known as COX. The COX enzyme helps the reaction

that prostaglandins. Blocking COX also interfere with platelets-cells in the blood involved in clotting. This is why NSAIDs have anti-clotting properties. In case of aspirin, this property helps prevent the blocked arteries that can cause heart attacks or stroke (13).

Classification

There are two types of NSAIDs available: Non-selective and COX-2 selective. Most NSAIDs are non-selective, and inhibit the activity of both COX-1 and COX-2. These NSAIDs, while reducing inflammation, also inhibits platelets aggregation (especially aspirin) and increase the risk of gastrointestinal ulcer/bleeds. COX-2 selective inhibitors have less gastrointestinal side effects, but promote thrombosis and substantially increase the risk of heart attack (14).

Mechanism Of Action

Inhibition of cyclooxygenase enzyme as the main mechanism of NSAIDs' analgesic, antipyretic, and anti-inflammatory properties (15) NSAIDs blocks COX enzymes and reduces production of prostaglandins. Therefore, inflammation, pain, and fever are reduced. Since the prostaglandins that protect the stomach and promote blood clotting also are reduced. NSAIDs that blocks both COX-1 and COX-2 can cause ulcer in stomach and intestines, and increase the risk of bleeding (16). NSAIDs promote sodium and water retention, and this has generally been explained by a reduction in prostaglandin induced inhibition of both renal chloride reabsorption and the action of antidiuretic hormones (17).

Aspirin

Aspirin is a prototype of non-steroidal anti-inflammatory drug (NSADs), and member of the family of salicylates that have in common salicylic acid as the active agents (18).

Mechanism of Action

Acetylsalicylic acid acts as an acetylating agent. Thus, aspirin irreversibly inactivates cyclooxygenase (COX)-1 and suppresses the generation of prostaglandin H₂ (a precursor of thromboxane A₂). Aspirin achieves this effect through its acetyl group, which becomes covalently attached to Ser529 of the active site of the COX-1 enzyme. Aspirin interacts with the amino acid Arg120 and consequently blocks the access of arachidonic acid to the hydrophobic channel to Tyr385 at the catalytic site. Thus, aspirin inhibits the generation of prostaglandin H₂ (19). Aspirin is readily absorbed in the acidic environment of the gastric mucosa. At this interface, aspirin can readily inhibit the biosynthesis of prostaglandins that are associated with protection of the stomach lining (20).

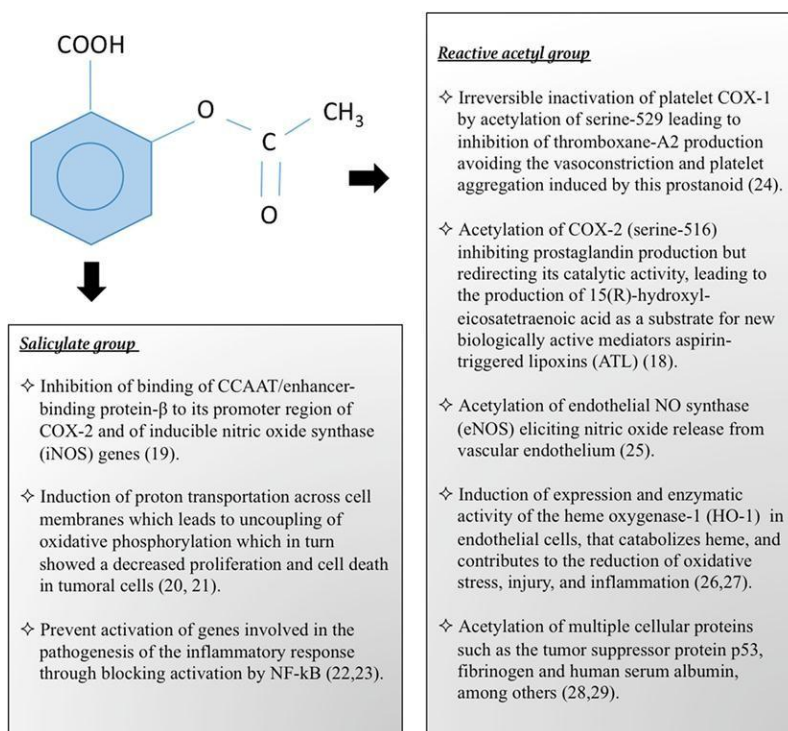


Fig.1; Mechanism of Action of Aspirin

Celecoxib

Celecoxib is Non-steroidal anti-inflammatory drug (NSAIDs) with anti-inflammatory, analgesic, and antipyretic properties. It is approved for the treatment of osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and acute pain. Celecoxib has also shown promise in prevention of cancer (21).

Mechanism of Action

The mechanism of action of celecoxib is due to selective inhibition of cyclooxygenase-2 (COX2) which is responsible for prostaglandin synthesis, an integral part of the pain and inflammation pathway. This activity gives celecoxib its analgesic, anti-inflammatory, and antipyretic activity. Celecoxib does weakly inhibit COX-1 and therefore, may affect platelet function to a lesser extent. Celecoxib also has anticancer property. Celecoxib is extensively metabolized through cytochrome P450 2C9 (CYP2C9) and may have interaction with other medication that are substrate of CYP2C9 (22)

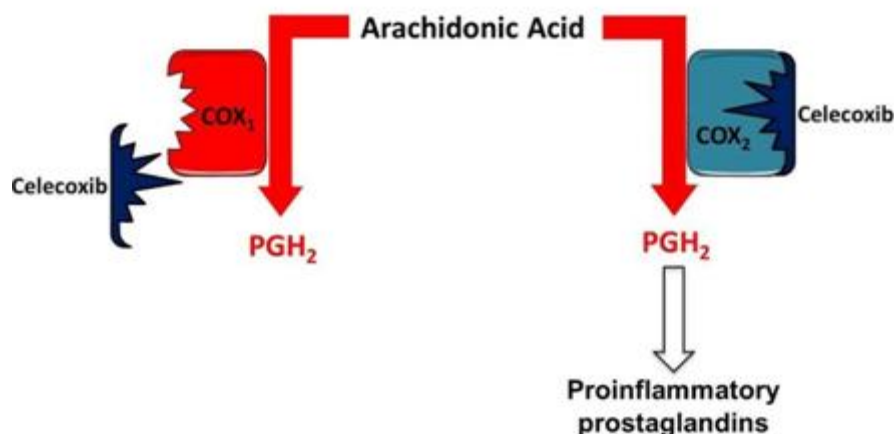


Fig.2: Mechanism of Action of Celecoxib

Side Effects of Celecoxib

Celecoxib, like other NSAIDs may cause serious stomach and intestinal ulcers that may occur at any time during treatment. Celecoxib does not interfere with the function of blood platelets and, as a result, does not reduce clotting and lead to increased bleeding time like other NSAIDs. Allergic reaction can occur with celecoxib (23).

NSAIDs' Known Adverse Effects

NSAIDs and Kidneys:

NSAIDs cause inhibition of prostaglandin and thromboxane synthesis leading to renal vasoconstriction and consequently reduced renal perfusion and aberrant renal function (24).

Peptic ulcer and gastrointestinal bleeding:

Long term or high dose use of NSAIDs could also lead to ulcers developing in the gut, known as peptic ulcer (25).

Blood:

Non-steroidal anti-inflammatory drugs (NSAIDs) can affect platelet aggregation and bleeding time due to inhibition of PG and TXA₂ synthesis. Aspirin is most potent compound in this respect due to the irreversible inhibition of COX-1 from the platelets, which translates into an increase in bleeding time (26).

Heart Failure:

Inhibition of prostanoid production in the kidney may reduce glomerular filtration and extraction of sodium and water. NSAIDs are therefore associated with risk of hypervolemia and worsening heart failure (27).

NSAIDs as Anti-cancer Agent:

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely prescribed for patients with coronary heart disease and rheumatoid arthritis. Currently, NSAIDs are becoming necessary in management of cancer patients. One important reason for the use of NSAIDs is that blood coagulation system is often activated in course of malignancies, and the risk of venous thromboembolism increases with locally advanced or metastatic cancer. Recently, NSAIDs are further recommended as the primary drug for prevention of colorectal cancer (28).

CONCLUSION:

Several important points can be made from this review. Firstly, the use of NSAIDs should be reserved for patients suffering from debilitating musculoskeletal condition such as osteoarthritis. Non-steroidal anti-inflammatory drugs (NSAIDs) including both Selective and Nonselective should be used with caution in patient with pre-existing cardiovascular condition and the physician should select the NSAID with the lowest possible risk to the patient's current condition. NSAIDs are one of the commonly prescribed drugs in the elderly. NSAIDs should be prescribed for the shortest duration possible in the lowest effective dose, and with careful surveillance to monitor GI, renal, and cardiovascular toxicity. Numerous experimental, clinical studies indicates that NSAIDs particularly the highly selective COX-2 inhibitors, show promise as anticancer drugs, but the clinical application of these drugs is still limited by the lack of randomized evidence.

REFERENCE:

- 1) Johani Fourie; A review of non-steroidal anti-inflammatory drug
- 2) Ki E Park, Yi Qin and Anthony A Barvy; Non-steroidal anti-inflammatory drug and their effect in elderly
- 3) <http://www.zana.com/a/non-steroidal-anti-inflammatory-drugs-introduction.289>
- 4) <http://www.ibdrelief.com/---/anti-inflammatories-non-steroidal-introduction>
- 5) <http://en.wikipedia.org/wiki/Anti-inflammatory>
- 6) Zoltan Varga, Syed rafay ali sabzwari, and Veronika Vargova; Cardiovascular Risk of Nonsteroidal Anti-Inflammatory Drugs: An Under Recognized Public Health Issue
- 7) <http://www.bmj.com/content/346/bmj.f3195>
- 8) <http://www.tga.gov.au/alert/non-steroidal-anti-inflammatory-drugs-nsaids-review>
- 9) Rajeshwary Ghoshi, Azra Alajbegovic, and Aldrin V. Gomes; Review Article, NSAIDs and Cardiovascular Disease: Role of Reaction Oxygen Species, Oxidative Medicine and Cellular Longevity Volume 2015.

- 10) <http://www.clinicalcorrelations.org/2018/02/01/nsaids-are-they-all-the-same/>
- 11) R Andrew Moore, Sheena Derry, Ceri J Phillips and Henry J Mc Quarry; Nonsteroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase-2 selective inhibitors (coxib) and gastrointestinal harm: review of clinical trials and clinical practice.
- 12) <http://www.cochrane.org/CD000396/BACK-non-steroidal-anti-inflammatory-drugs-for-lowback-pain>
- 13) Medicalnewatodat.com/articles/179211.php
- 14) en.wikipedia.org/wiki/Nonsteroidal-anti-inflammatory-drug
- 15) Newman Osafo, Christian Agyare, David Darko Obiri and AaronOpoku Antwi; Mechanism of Action Nonsteroidal Anti-Inflammatory Drugs.
- 16) [rxlist.com/nsaids-nonsteroidal-anti-inflammatory-drugs/drugs condition.htm](http://rxlist.com/nsaids-nonsteroidal-anti-inflammatory-drugs/drugs_condition.htm)
- 17) Kathleen M Knights, Arduino A Mangoni, and John O Miners; Non-selective nonsteroidal anti-inflammatory drugs and cardiovascular events: is aldosterone the silent partner in crime?
- 18) Angela P. Cadavid; Aspirin: The Mechanism of Action Revisited in the Context of Pregnancy Complications.
- 19) Mekaj Y, Daci F, Mekal A; New insight into the mechanism of action of aspirin and its use in the prevention treatment of arterial and venous thromboembolism.
- 20) Argentina Ornelas, Niki Zacherias Millward, David G. Menter, Jannifer S. Davis, Lenard Linchtenberger, David Hawke, Ernest Hawke, Eduardo Vilar, Pratip Bhattacharya, Steven Millward; Beyond COX-1: the effect of aspirin on platelet biology and potential mechanism of chemoprevention.
- 21) Li Gong, Caroline F. Thorn, Monica M. Bertagnolli, Tilo Grosser, Russ B. Altman and Teri E. Klein; Celecoxib Pathway: Pharmacokinetics and Pharmacodynamics.
- 22) Brandon Cohen; Charles V. Preuss; Celecoxib.
- 23) medicinenet.com/celecoxib/article.htm#what_are_the_side_effects_of_celecoxib
- 24) Supakanya wongrakpanich, Amraporn Wongrakpanich, Katie Melhado and Jahani Rangaswani; A Comprehensive Review of Non-Steroidal Anti-Inflammatory Drug Use in The Elderly.
- 25) Markus MacGill; Everything you need to know about NSAIDs.
- 26) Oloviu Vostinaru; Adverse Effects and Drug Interactions of the Non-Steroidal AntiInflammatory Drugs.

- 27) Zoltan Varga, Syed rafay ali Sabzwari and Veronika Vargova; Cardiovascular Risk of Nosteroidal Anti-Inflammatory Drugs: An Under Recognized Public Health Issue.
- 28) Xiaoping Zhao, ZhiXu and Haoseng Li; NSAIDs Use and Reduced metastasis in Cancer Patients: results from a meta-analysis.