



**Libyan International Medical University**  
**Faculty of Basic Medical Science**



**The Beneficial Effects of Aspirin in Cardiovascular Disease Prevention**

- ❖ **Submitted by:** Ragheda Mohamed Ezwaie, Second Year Student, Faculty of Basic Medical Science, Libyan International Medical University.
- ❖ **Supervisor:** Dr. Rasha Giumma Hussien, Tutor, Faculty of Basic Medical Science, Libyan International Medical University.
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## **Summary (Abstract):**

The spectrum of acute coronary syndromes including unstable angina, non-ST segment elevation myocardial infarction (MI), ST segment elevation MI, and sudden cardiac death account for more than two million hospitalizations and 30% of all deaths in the U.S. each year. Aspirin produces statistically significant and important reduction in cardiovascular disease morbidity and mortality among survivors of a wide range of occlusive cardiovascular disease events. The majority of acute coronary syndromes are caused by atherosclerotic plaque rupture, which platelets play a significant role in its pathophysiology, and aspirin is the most commonly used antiplatelet agent in terms of prevention of cardiovascular diseases. This report demonstrates the different mechanisms by which aspirin inhibits platelet function and aggregation at the site of endothelial injury, and the possible antioxidant properties of aspirin.

## **1. Introduction:**

**1.1. The Definition of Aspirin:** Aspirin, also known as acetylsalicylic acid (ASA), is a non-steroidal anti-inflammatory drug (NSAID) which has long been heralded that its daily use, particularly in adults aged 50 to 69 years,<sup>1</sup> has significant cardioprotective effects, which is demonstrated clinically in the primary and secondary prevention of myocardial infarction, stroke, heart attacks, and cardiovascular death, by antagonizing platelets function.<sup>2</sup>

**1.2. The Definition of Atherosclerosis:** Atherosclerosis is a degenerative disease characterized by the formation of plaques in the inner layer of arteries. This disease causes the majority of acute coronary syndromes by rupture or fissuring of these plaques and the subsequent occlusive or subocclusive thrombus formation.<sup>3</sup>

**1.3. The Role of Platelets in Atherosclerosis:** Platelets main role comes when the rupture of the atherosclerotic plaques causes exposure of the content of the lipid core and promote platelets adhesion and activation of the extrinsic coagulation cascade. The activated platelets then release a variety of vasoactive substances including, thromboxane (TX) A<sub>2</sub> and adenosine diphosphate, (ADP) that promote primary homeostasis. Secondary homeostasis occurs as a result of thrombin-mediated conversion of fibrinogen to fibrin and subsequent stabilization of the platelet aggregate.<sup>3</sup>

## **2. The Role of Aspirin in Cardiovascular Disease Prevention:**

### **2.1. The Anti-inflammatory Effects of Aspirin:**

A recent meta-analysis reported that, among high-risk vascular patients, aspirin therapy was associated with a 34% reduction in nonfatal MI, a 25% reduction in nonfatal stroke, and an 18% reduction in all-cause mortality, however, the risk of recurrent vascular events among patients taking aspirin remains relatively high. Aspirin achieves its primary antithrombotic effect by interfering with platelet aggregation, and this is done by the inactivation of cyclooxygenase (COX), a key enzyme in platelet arachidonic acid metabolism. More specifically, aspirin inhibits the COX activity of prostaglandin (PG) H-synthase by acetylation of a single serine residue at position 529 (ser<sup>529</sup>) within this enzyme. This in turn blocks the metabolism of arachidonic acid to prostaglandin H<sub>2</sub>(PGH<sub>2</sub>), which is the precursor of thromboxane A<sub>2</sub> (TXA<sub>2</sub>) and other

cyclic prostaglandins. In human platelets, TXA<sub>2</sub> is synthesized and released in response to various stimuli and works by amplifying the activating signal, promotion of irreversible platelet aggregation and causes vasoconstriction.<sup>3</sup>

There are two COX isoforms, but only the first (COX-1) is constitutively expressed in mature platelets, and because platelets have minimal capacity for protein synthesis, the inactivation of COX-1 by aspirin is irreversible for the life of the platelets (8-10 days). The second isoform (COX-2) is inducible in newly formed platelets (8% to 10% of circulating platelets), hence, the inactivation of this form by aspirin causes decrease in the production of COX-2- derived TXA<sub>2</sub>.<sup>3</sup> The relatively weak anti-inflammatory effect of aspirin at low doses is in part explained by the fact that aspirin has 170-fold more potent inhibition of COX-1 than COX-2, and in part by the inhibitory effect of aspirin on endothelium-derived prostacyclin (PGI<sub>2</sub>), which is released by vascular endothelium as an endogenous mechanism to prevent platelet adhesion and aggregation. And because endothelial cells rapidly recover COX activity, unlike platelets, and make this aspirin-mediated effect short-lived, dose-dependent, and perhaps less important when compared to the antiplatelet effect.<sup>3</sup>

## **2.2. The Non-prostaglandin-mediated Effects of Aspirin:**

There are non-prostaglandin-mediated effects of aspirin that influence homeostasis, that are dose-dependent and unrelated to COX-1 activity, including vitamin K antagonism, decrease platelet production of thrombin, acetylation of one or more clotting factors, and inhibition of neutrophil-mediated platelet activation.<sup>3</sup>

Aspirin is a fast and efficient (OH<sup>-</sup>) radical scavenger by working as an antioxidant. And this antioxidant property of aspirin exhibits a protective effect against silica-induced lipid peroxidation, DNA strand breakage, and silica-induced transcription factor-kb activation. Also the low-dose aspirin therapy has been reported to be more sufficient in preventing MI in men with higher C-reactive protein levels than in those with lower levels, raising the possibility that aspirin prevents thrombosis by reducing vascular inflammation.<sup>4</sup>

### **Conclusion:**

The daily use of aspirin in adults aged from 50-69 years, who are at increased risk of cardiovascular diseases or have a history of cardiovascular diseases, has an important protective effect. Aspirin is the most commonly used antiplatelet agent that its cardioprotective function have been proved, particularly, by inhibiting COX enzymes and preventing subsequent events.

### **References:**

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