Abstract
The cyclooxygenase enzyme (COX), also known as prostaglandin H2 synthase (PGHS or PES) has a role in the formation of eicosanoid inflammatory mediators such as prostaglandins, prostacyclins and thromboxanes.

The first and committed step in the production of prostaglandins occurs in the COX active site and involves the addition of two oxygen molecules to arachidonate to form hydroperoxy endoperoxide prostaglandin G2 (PGG2). PGG2 is then reduced to prostaglandin H2 (PGH2) in the peroxidase active site.

Eicosanoids are involved in numerous physiologic processes such as platelet activation, inflammation, pain, and fever. Aspirin is used to reduce the physiologic effect of the eicosanoids within the human body.

Introduction
Aspirin's target is the COX enzyme; two slightly different versions exist.

• COX-1, has irreversible binding
• COX-2, has reversible binding
• COX-1 and COX-2 have an impact on pain and inflammation
• Only inhibition of COX-1 contributes to platelet inactivation
• As a platelet inhibitor, ASA is preventative against stroke and heart attack

Aspirin inhibits the COX enzyme by acetylating a hydroxy group in the enzyme's active site. Acetylation of the COX-1 and COX-2 active sites does not produce the same inhibitory effects.

• A serine residue is acetylated in both COX-1 and COX-2 but the two COX sites differ in exact amino acid sequence
• Arachidonate is irreversibly inhibited from entering the COX-1 active site after aspirin acetylates the Ser-530 residue
• Due to irreversible inhibition of COX-1, a new enzyme must be transcribed before more prostaglandins are produced
• The active site of COX-2 is larger than that of COX-1, which is why irreversible inhibition does not occur in COX-2
• Aspirin's irreversible inhibition of COX-1 prevents platelets from producing Thromboxane A2 (TxA2)
• TxA2 is necessary for platelet activation and recruitment

Aspirin and the Future
Cancer Prevention
Aspirin has shown promise in preventing cancer. In a trial spanning 2 years, colon cancer risk was reduced by 63% in patients taking daily aspirin. The proposed mechanism is that aspirin helps induction of apoptotic pathways by damaged/mismatched DNA.

Aspirin Derivatives
Nitric oxide donating aspirin derivatives have shown promise in protecting against gastric damage, a common side effect of COX-1 inhibition. The inhibition of neutrophil adherence by NO is the proposed mechanism.

Summary
A vast array of NSAIDs are currently on the market, including aspirin. Aspirin is one of the oldest and most commonly used among its class. Aspirin's anti-inflammatory, anti-inflammatory and antiplatelet effects make it arguably the most widely used drug in the world.

The inhibition aspirin exerts on COX-1 has advanced the common saying; an aspirin a day keeps the doctor away, two aspirin a day doubles the chances of a long life. Additionally, aspirin has a promising future in the treatment and management of evolving inflammatory diseases.

References: