

# **Cyclooxygenase: COX-1 and COX-2 Explained**

## ***What You Need to Know About Cyclooxygenase***

By Carol Eustice

### **What Is Cyclooxygenase (COX)?**

Cyclooxygenase (COX) is an enzyme that is responsible for the formation of prostanoids. The three main groups of prostanoids -- prostaglandins, prostacyclins, and thromboxanes -- are each involved in the inflammatory response.

### **Two Forms of Cyclooxygenase (COX)**

In the 1990s, researchers discovered that two different COX enzymes existed, now known as COX-1 and COX-2. Cyclooxygenase-1 (COX-1) is known to be present in most tissues. In the gastrointestinal tract, COX-1 maintains the normal lining of the stomach. The enzyme is also involved in kidney and platelet function. Cyclooxygenase-2 (COX-2) is primarily present at sites of inflammation.

While both COX-1 and COX-2 convert arachidonic acid to prostaglandin, resulting in pain and inflammation, their other functions make inhibition of COX-1 undesirable while inhibition of COX-2 is considered desirable.

### **NSAIDs Inhibit COX**

Nonsteroidal anti-inflammatory drugs (NSAIDs), commonly prescribed to treat arthritis, work by inhibiting prostaglandins. Traditional NSAIDs (ibuprofen, naproxen), however, can cause gastrointestinal problems including ulcers.

Traditional NSAIDs are considered "nonselective" because they inhibit both COX-1 and COX-2. The inhibition of COX-2 by traditional NSAIDs accounts for the anti-inflammatory effect of the drugs while the inhibition of COX-1 can lead to NSAID toxicity and associated side effects (ulcers, prolonged bleeding time, kidney problems).

### **COX-2 Selective NSAIDs**

In the late 1990s, the first COX-2 selective NSAID (Celebrex) was developed, and others soon followed. Theoretically, drugs which were developed as COX-2 selective inhibitors -- Celebrex, Vioxx, and Bextra -- should have been preferred over traditional NSAIDs.

Vioxx and Bextra have since been removed from the market, and Celebrex remains the only available COX-2 inhibitor available in the United States. Since the withdrawal of Vioxx, due to an increased risk of heart attack and stroke, the FDA scrutinized the entire class of drugs (all NSAIDs and COX-2 inhibitors, sold over-the-counter or by prescription only) and added warnings to the prescribing instructions.

- Vioxx Recalled in September 2004
- Bextra Withdrawn in April 2005

Two other COX-2 inhibitors in development, Arcoxia and Prexige, have so far been rejected by the FDA. Prexige has also been removed from the market in Australia and Canada due to related liver complications.

Some researchers believe, after finding low levels of COX-2 in some non-inflamed tissue, that COX-2 may also play a role in certain normal functions of the body other than inflammation. While NSAIDs and COX-2 inhibitors are considered significant treatment options for arthritis patients, the benefit and risks must be considered for each individual patient.