Abstract

Cyclo-oxygenase-2 (COX-2), a rate-limiting enzyme for prostanoid synthesis, is induced during inflammation and participates in inflammation-mediated cytotoxicity. The discovery of two cyclo-oxygenase (COX) isoenzymes, viz. COX-1 and COX-2, has updated the knowledge of non steroidal anti-inflammatory drugs (NSAIDs). The two COX isoenzymes share structural and enzymatic similarities, but are specifically regulated at the molecular level and may be distinguished apart in their functions, although some physiological overlap between them does occur. The major goal in developing selective COX inhibitors is to improve NSAID tolerability. Conventional non steroidal anti-inflammatory drugs (NSAIDs) nonspecifically inhibit cyclooxygenase-1 (COX-1), an enzyme critical to normal platelet function, and COX-2 which mediates inflammatory response mechanisms. Celecoxib, the 1, 5-diarylpyrazole compounds was the first launched selective COX-2 inhibitor, and has excellent selectivity and potent anti-inflammatory activity. COX-2 is required for both the constitutive and mitogen-induced PGE2 synthesis. Moreover, over-expression and persistent expression of COX-2 may be influenced by breast tumor hormone status and seem to be a feature of the aggressive,
Recent studies have indicated that the relationships between polyunsaturated fatty acid metabolism and carcinogenesis have led to new targets for the design of mechanism based drugs in cancer chemoprevention research. Selective inhibition of COX-2 provided a new class of anti-inflammatory, analgesic, and antipyretic drugs with significantly reduced side effects. It has been reported that inhibiting COX-2 could also be an important strategy for preventing or treating a number of cancers. COX-2 selective inhibitors such as celecoxib, rofecoxib and valdecoxib are currently being used to reduce inflammatory response. However, they lack anti-thrombotic activity and hence lead to cardiovascular and renal liabilities apart from gastrointestinal irritation. Therefore, there is still a need to develop more potent COX-2 inhibitors. One of the keys to developing COX-2 selective drugs is the larger active site of COX-2, which makes it possible to make molecules too large to fit into the COX-1 active site but still able to fit the COX-2.

References

11. www.arkat-usa.org
Index Terms

Computer Science  Applied Sciences

Keywords

COX-2, Phylogenetic tree, Correlation, Inhibitors.