Objectives of present Research work:

The quest for better safer and potent anticancer agents is a continuous process. Almost all currently available antineoplastic agents are suffering from one or more adverse effect. To cope with the current requirement in the present research project, we have tried to explore the clinically available COX-2 inhibitors and newly developed new chemical entities not only for their anti-inflammatory activity but also as anticancer activity to inhibit COX-2 and LOX leading to induction of apoptosis and thus can be used as anticancer agents.

Recently, selective inhibitors of the COX-2 isoform have attracted considerable attention because of their ability to selectively inhibit the inducible COX-2 isoform. This significantly reduces the gastrointestinal and renal side effects of NSAIDs, which have greatly limited the wide use of these drugs as chemopreventive agents. The mechanism by which these drugs inhibit tumor growth and progression is unclear, and our knowledge about their potential in prostate cancer therapy is far from adequate.

Therefore we thought it worth optimizing the structural features responsible for anti cancer activity by molecular modeling studies of reported selective COX-2 inhibitors as anticancer agents.

The development of safe and effective drugs for chemoprevention is complicated by the potential of even rare, serious toxicity to offset the benefit of treatment, particularly when the drug is administered to healthy people who have low annual risk of developing the disease for which treatment is intended. This project considers generic approaches to improve the balance between benefits and risks associated with the use of NSAIDs in chemoprevention.
Numerous experimental, epidemiologic, and clinical studies suggest that nonsteroidal anti-inflammatory drugs (NSAIDs), particularly the highly selective cyclooxygenase (COX)-2 inhibitors, have promise as anticancer agents. NSAIDs restore normal apoptosis in human adenomatous colorectal polyps and in various cancer cell lines that have lost adenomatous polyposis coli gene function. NSAIDs also inhibit angiogenesis in cell culture and rodent models of angiogenesis. Many epidemiologic studies have found that long-term use of NSAIDs is associated with a lower risk of colorectal cancer, adenomatous polyps, and, to some extent, other cancers\(^1\).

COX-2 inhibitors are implicated to possess a broad therapeutic spectrum besides anti-inflammatory, analgesic and to lesser extent antipyretic activities. For example inhibition of COX-2 can prevent growth of certain types of cancer, especially colon cancer. The expression of COX-2 in brain, kidney and bone marrow has made it an attractive therapeutic target for designing selective drugs for Alzheimer's disease, cancer etc. The efficacy of these drugs is proven to be better than that of traditional NSAIDs, with no or little side effects associated with traditional NSAIDs\(^2\).