

## 1.4 Cyclooxygenase Isoforms

Cyclooxygenases exist in three distinct isoforms, a constitutive form (COX-1), inducible form (COX-2) and COX-3. The COX-1 enzyme is expressed in resting cells of most tissues, functioning as a housekeeping enzyme, and is responsible for maintaining homeostasis (gastric and renal integrity) and normal production of prostaglandins. COX-2 is predominantly found in brain, kidney and endothelial cells, but is virtually absent in most other tissues. However, COX-2 expression is significantly up regulated as a part of various acute and chronic inflammatory conditions, and in neoplastic tissues. (Sharma, S. K., 2012).

More recently, a novel COX-1 splice variant termed as COX-3 has been reported. COX-3 is an enzyme that is encoded by the COX-1 gene, with difference that COX-3 retains an intron that is not retained in COX-1. (Botting R. 2003, Baker Jawabrah, 2012).

Two smaller COX-1 derived proteins, partial COX-1a (PCOX-1a) and partial COX-1b (PCOX-1b) variants have been found. Both derivatives have been shown not to be involved in prostaglandins synthesis and their function still need to be identified. (Chandraskharan et al 2002).

Each enzyme has four domains: the dimerization domain, epidermal growth factor domain, membrane binding domain and the catalytic domain. The catalytic domain has the cyclooxygenase active site and peroxidase active site. The cyclooxygenase active site is long, narrow channel of largely hydrophobic character that opens in the membrane binding domain.