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Cyclooxygenase-2 and 15-lipoxygenase inhibition, synthesis, anti-inflammatory activity and ulcer liability of new celecoxib analogues: Determination of region-specific pyrazole ring formation by NOESY.

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Abstract — Two new series of 1,5-diaryl pyrazoline (**3a-f**) and 1,5-diaryl pyrazole (**5a** and **5b**) were designed as both COX -2 and 15-LOX inhibitors. All the prepared compounds were fully characterized by all spectral and element analysis. Their anti-inflammatory activity and ulcer index were included. Pyrazoline **3f** is the most effective with IC_{50} = 1.14 & 4.7 µM against COX-2 and 15-LOX respectively, and more potent than celecoxib and meclofenamate references. In addition **3a**, **3b**, **5a,** and **5b** were safer with low ulcer index than celecoxib. Docking study was performed for the most active compounds such as **2b**, **3a,** and **3f** on COX-2 and 15-LOX enzymes.

Prostaglandins (PGs), prostacyclin (PGI_2), thromboxanes (TXA_2), and leukotrienes (LTs) are some metabolites of arachidonic acid (AA). Arachidonic acid is the most abundant polyunsaturated fatty acid bound to cell membranes. PGs and PGI_2 are produced through cyclooxgenase (COX) pathway type [1-3]. Cyclooxygenase isozymes are classed into a constitutive COX-1, an induced COX-2, and COX-3 that remains under investigation. In contrast, leukotrienes (LTs) are the final metabolites of AA *via* LOX pathway [4]. There are four different