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# 2-Aryl quinolines related to some nsaids are selective COX-2 inhibitors

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**Background and Aims:** Cyclooxygenase-2 (COX-2) has a key role in inflammatory disorders such as rheumatoid arthritis and osteoarthritis, and it is also implicated in cancer and angiogenesis. In this regard, several epidemiologic studies have been reported that inhibitors of COX-2 enzyme reduce the risk of colorectal, breast, and lung cancer, and COX-2 is expressed in these cancers. As a consequence, increasing interest has been devoted to the synthesis of selective inhibitors of COX-2 by means of modification of well-known non-selective agents (NSAIDs), so in this study 2-aryl quinolines were designed, synthesized and evaluated as COX-2 inhibitors, using some NSAIDs, (naproxen, flurbipropen, ibuprofen and ketoprofen) as lead compounds.
**Methods:** 2-aryl quinolines possessing a methylsulfonyl or azido COX-2 pharmacophore at the para position of the C-2 phenyl ring Were designed as COX-2 inhibitors, using some NSAIDs, (naproxen, flurbipropen, ibuprofen and ketoprofen) as lead compounds. Doebner reaction was used to prepare the target 2-arylquinolines; 4-substituted benzaldehyde, pyruvic acid and an appropriate amine were heated in ethanol and in some cases in acetic acid to provide 2-aryl quinolines and then oxidation of the methylthio substituent to a methylsulfonyl substituent was carried out using Oxone. Hydrolysis of acetamido derivatives under acidic condition gave the corresponding amines. Diazotization of 2-p-amino quinoline with sodium nitrite followed by treatment with sodium azide afforded the azide derivatives. The ability of the test compounds to inhibit ovine COX-1 and COX-2 was determined using chemiluminescent enzyme assays kit.
**Conclusions:** This study indicates that (i) in this class of compounds COX-1/-2 inhibition is sensitive to the lipophilic nature of the C-7 and C-8 quinoline substituents, and(ii) COX-1/COX-2 inhibition is very sensitive to the substituent of the para position of C-2 phenyl ring, (iii) COX-1/COX-2 inhibition is affected by the position of benzoyl moiety on the quinoline ring.

**Keywords:** Quinoline; COX-2 inhibitor; NSAIDS