J Pain Relief 2017, 6:5(Suppl)
DOI: 10.4172/2167-0846-C1-015

Synthesis, molecular docking and biological evaluation of some 2-substituted-6-(morpholin-4-yl) pyridazin-3(2h)-ones as potent anti-inflammatory and analgesic agents

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Inflammation is a body response to injury or abnormal stimulation caused by a physical, chemical or biological agent. The first-line mode of therapeutic intervention for inflammation is non-steroidal anti-inflammatory drugs(NSAIDs). However, the long-term use of NSAIDs produces high incidence of gastrointestinal irritation, resulting in the development of life-threatening gastrointestinal side effects such as gastric irritation, ulceration and bleeding. Further discovery of selective COX-2 inhibitors (coxibs) suggested safety without any ulcerogenic side effects; however, long-term use of these drugs resulted in kidney and hepatic toxicity along with an increased risk of secondary cardiovascular effects. Therefore, development of novel anti-inflammatory agents with an improved safety profile is still a necessity to overcome the side effects of the existing agents. The basic approaches towards inflammation and pain treatment are constantly changing and researchers are continuously trying to develop safer and effective anti-inflammatory drug candidates for the treatment of different inflammatory conditions such as osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, psoriasis and multiple sclerosis. Synthetic 3(2H)-pyridazinones constitute an important scaffold for drug discovery. Docking studies suggest that introduction of morpholine moiety on the 6-position and attachment of an amide at N-2 position of pyridazinone nucleus through a methylene spacer may lead to products having potent analgesic

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