World Academy of Science, Engineering and Technology
International Journal of Pharmacological and Pharmaceutical Sciences
Vol:14, No:03, 2020

# Synthesis of Quinazoline Derivatives as Selective Inhibitors of Cyclooxygenase-1 Enzyme

**Authors :** Marcela Dvorakova, Lenka Langhansova, Premysl Landa

**Abstract :** A series of quinazoline derivatives bearing aromatic rings in 2- and 4-positions were prepared and tested for their biological activity. Firstly, the compounds were evaluated for their potential to inhibit various kinases, such as autophagy activating kinase ULK1, 3-Phosphoinositide-dependent kinase 1, and TANK-binding kinase 1. None of the compounds displayed any activity on these kinases. Secondly, the compounds were tested for their anti-inflammatory activity expressed as cyclooxygenase (COX) isoforms and 5-lipoxygenase (5-LOX) inhibition. Three of the compounds showed significant selectivity towards COX-1 isoform (COX-2/COX-1 SI = 20-30). They inhibited COX-1 in a single-digit μM range. There was also one compound that exhibited inhibitory activity towards all three tested enzymes in μM range (IC50COX-1 = 1.9 μM; IC50COX-2 and 5-LOX = 10.1μM. COX-1 inhibition was until recently considered undesirable due to COX-1 constitutive expression in most cell types and tissues. Thus, there are not many compounds known with selective COX-1 activity. However, it is now believed that COX-1 plays an important role in the pathophysiology of several acute and chronic disorders, including cancer or neurodegenerative diseases. Thus, the discovery of effective COX-1 selective inhibitors is desirable and important.

**Keywords :** cyclooxygenases, kinases, lipoxygenases, quinazolines
**Conference Title :** ICBCP 2020 : International Conference on Biochemical and Clinical Pharmacology
**Conference Location :** Rome, Italy
**Conference Dates :** March 05-06, 2020