

A preclinical profiling of a promising drug candidate for rheumatoid arthritis

Gopalan Kutty Nampurath, Jayesh Mudgal and Vasantharaju S Gowdra
Manipal University, India

A recent report from our lab has claimed the remedial effect of three thiazolidin-4-ones against chemical mediated inflammation. Out of these molecules, [2-(4-chlorophenoxy)-N-(5-methyl-4-oxo-2(pyridin-2-yl) thiazolidin-3-yl) acetamide] (4C), corrected the inflammatory condition through inhibition of the major biomarkers of inflammation and pain such as cytokines (TNF- α and IL-6) and prostaglandin (PGE2) generation. This prompted the evaluation of its anti-inflammatory/antirheumatic effect in an experimental model of arthritis in the present study. After securing ethical clearance, experimental arthritis was induced in Sprague-Dawley rats using sub-plantar injection of complete Freund's adjuvant (CFA). On Day 14 after CFA injection, animals were randomized and divided into different treatment groups (n=6) based upon the inflammation produced in contra lateral paw (un-injected paw). Treatment with compound 4C inhibited the progression of chronic inflammation and reduced the associated pain sensation in rats. The compound was found effective against polyarthritic condition in rats. In accordance with previous findings, 4C inhibited the generation of pro-inflammatory cytokines (TNF- α and IL-6) and PGE2 in the current experimental model of arthritis. In the earlier work on 4C, we reported the inhibition of COX-2 *in vitro* and inhibition of PGE2 generation in rat air pouch model. Thus, the mechanisms of anti-inflammatory and analgesic activities of the molecule have been established. In addition, results revealed that compound 4C was safer than diclofenac in terms of side effects such as gastric toxicity, renal toxicity, thrombocytopenia and hypertriglyceridemia that were observed in the current study. The results of study suggest the local and systemic ameliorative effect of oral 4C in arthritis condition.

Biography

Gopalan Kutty Nampurath Ph.D is a Professor of pharmacology at Manipal College of Pharmaceutical Sciences, Manipal University, Manipal, India. He has research experience of 25 years and has published 31 papers in reputed journals. His areas of research interest are inflammation, dyslipidemia and diabetes. He guided six PhDs and over 50 Postgraduate students. He has peer-reviewed papers for international journals like *European Journal of Medicinal Chemistry*, *Pharmaceutical Biology*, and *Indian Journal of Pharmacology* etc.

ng.kutty@manipal.edu

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