Biological evaluation and molecular docking studies of novel 1,3,4-oxadiazole derivatives of 4,6-dimethyl-2-sulfanylpyridine-3-carboxamide.

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To date, chronic inflammation is involved in most main human pathologies such as cancer, and autoimmune, cardiovascular or neurodegenerative disorders. Studies suggest that different prostanoids, especially prostaglandin E2, and their own synthase (cyclooxygenase enzyme-COX) can promote tumor growth by activating signaling pathways which control cell proliferation, migration, apoptosis, and angiogenesis. Non-steroidal anti-inflammatory drugs (NSAIDs) are used, alongside corticosteroids, to treat inflammatory symptoms particularly in all chronic diseases. However, their
toxicity from COX inhibition and the suppression of physiologically important prostaglandins limits their use. Therefore,in continuation of our efforts in the development of potent, safe, non-toxic chemopreventive compounds, we report herein the design, synthesis, biological evaluation of new series of Schiff base-type hybrid compounds containing differently substituted N-acyl hydrazone moieties, 1,3,4-oxadiazole ring, and 4,6-dimethylpyridine core. The anti-COX-1/COX-2, antioxidant and anticancer activities were studied. Schiff base 13, containing 2-bromobenzylidene residue inhibited the activity of both isoenzymes, COX-1 and COX-2 at a lower concentration than standard drugs, and its COX-2/COX-1 selectivity ratio was similar to meloxicam. Furthermore, the results of cytotoxicity assay indicated that all of the tested compounds exhibited potent anti-cancer activity against A549, MCF-7, LoVo, and LoVo/Dx cell lines, compared with piroxicam and meloxicam.Moreover, our experimental study was supported by density functional theory (DFT) and molecular docking to describe the binding mode of new structures to cyclooxygenase.