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Novel N-Aryl Indolylsulfoximines

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Abstract

A study of design, synthesis and promising selective anticancer agents The indole core continues to captivate researchers and remains a vibrant area of investigation due to its remarkable pharmacological potential. Both natural and synthetic indole-based compounds have garnered significant attention owing to their diverse biological activities, including antiviral, anti-inflammatory, anticancer, anti-HIV, antioxidant, antitubercular, antidiabetic, and antimalarial properties. This wide spectrum of bioactivity has spurred intense interest in the synthesis of novel indole derivatives. Meanwhile, sulfoximine derivatives have recently emerged as promising scaffolds in medicinal and synthetic chemistry, attracting growing interest from researchers in these fields. The combination of these two important chemical moieties, indoles and sulfoximines, offers a unique opportunity to develop novel compounds with potentially enhanced biological activities and therapeutic applications. As part of our efforts to develop novel anticancer agents, in the present work we have successfully synthesized and conducted cytotoxicity studies on indolylsulfoximines. A facile and efficient approach utilizing copper-mediated cross-coupling reaction of N-boc-3-indolylsulfoximines with aryl iodides was developed to synthesize a diverse range of N-arylated indolylsulfoximines in excellent yields (up to 91%). Indolylsulfoximines were readily prepared by the treatment of N-boc-3-methylthioindoles with a combination of IBD and ammonium carbamate. The reaction is highly chemoselective and tolerant of a wide range of functional groups. The prepared indolylsulfoximines are well characterized using NMR and Mass spectrometry. The N-arylated indolylsulfoximines derivatives displayed a broad spectrum of activity (1.2-8.2 M) against the tested prostate and breast cancer cell lines. These compounds were found to be non-cytotoxic to normal HEK293 cells, indicating their potential selectivity for cancer cells. Cellular assay shows that indolylsulfoximine increases the endogenous level of ROS, leading to the increased level of p-53 and c-jun inducing apoptosis. N-arylated indolylsulfoximines also induced mitochondrial dysfunction, further promoting apoptotic pathways. As oxidative stress causing tubulin depolymerization. Our data shows that N-aryl indolylsulfoximines could serve as potent and selective anti-cancer agents. A comprehensive presentation of the synthesis and the biological results of indolylsulfoximines will be delivered during the conference.