

## Synthesis and Anticancer Evaluation of Substituted 2-(3,4-Dimethoxyphenyl) Benzazoles

**Authors :** Cigdem Karaaslan, Yalcin Duydu, Aylin Ustundag, Can Ozgur Yalcin, Hakan Goker

**Abstract :** Benzazole nucleus is found in the structure of many compounds as anticancer agents. Bendamustine (Alkylating agent), Nocodazole (Mitotic inhibitor), Veliparib (PARP inhibitor), Glasdegib (SMO inhibitor) are clinically used as anticancer therapeutics which bearing benzimidazole moiety. Based on the principle of bioisosterism in the present work, 23 compounds belonging to 2-(3,4-dimethoxy-phenyl) benzazoles and imidazopyridine series were synthesized and evaluated for their anticancer activities. N-(5-Chloro-2-hydroxyphenyl)-3,4-dimethoxybenzamide, was obtained by the amidation of 2-hydroxy-5-chloroaniline with 3,4-dimethoxybenzoic acid by using 1,1'-carbonyldiimidazole. Cyclization of benzamide derivative to benzoxazole, was achieved by p-toluenesulfonic acid. Other 1H-benz (or pyrido) azoles were prepared by the reaction between 2-aminothiophenol, o-phenylenediamine, o-pyridinediamine with sodium metabisulfite adduct of 3,4-dimethoxybenzaldehyde. The NMR assignments of the dimethoxy groups were established by the Nuclear Overhauser Effect Spectroscopy. A compound named, 5(4),7(6)-Dichloro-2-(3,4-dimethoxy) phenyl-1H-benzimidazole, bearing two chlorine atoms at the 5(4) and 7(6) positions of the benzene moiety of benzimidazole was found the most potent analogue, against A549 cells with the GI<sub>50</sub> value of 1.5 µg/mL. In addition, 2-(3,4-Dimethoxyphenyl)-5,6-dimethyl-1H-benzimidazole showed remarkable cell growth inhibition against MCF-7 and HeLa cells with the GI<sub>50</sub> values of 7 and 5.5 µg/mL, respectively. It could be concluded that introduction of di-chloro atoms at the phenyl ring of 2-(3,4-dimethoxyphenyl)-1H-benzimidazoles increase significant cytotoxicity to selected human tumor cell lines in comparison to other all benzazoles synthesized in this study. Unsubstituted 2-(3,4-dimethoxyphenyl) imidazopyridines also gave the good inhibitory profile against A549 and HeLa cells.

**Keywords :** 3,4-Dimethoxyphenyl, 1H-benzimidazole, benzazole, imidazopyridine

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