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Synthesis and cytotoxic properties of new derivatives of dicarboximides

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The growth rate of the number of cancer cases is enormous and requires intensive research and introduction of new anticancer drugs. Ideally, these new drugs should possess improved pharmacokinetic parameters and high selectivity towards cancer cells providing less negative side effects. The present work describes the synthesis and cytotoxic activity of a large group of new derivatives of dicarboximides. In our previous studies with this group of compounds we have identified several derivatives that presented highest cytotoxicity to leukemia cells, lines K562, HL-60, respectively (IC50* in the range of 1-10μM). On the contrary, these compounds were non-toxic to non-tumor endothelial cells (HUVEC) and tumor adherent cells (HeLa). Considering the high activity of evaluated compounds, we decided to continue our work in the field of these derivatives. The main stage of synthetic works was the modification of the structure of dicarboximides to obtain products with improved solubility and bioavailability, while retaining their biological activity. To improve the solubility of the compounds hydrophilic groups such as -OH, -NH2, -NH-R were introduced to their structure. Thus, we have synthesized 33 new derivatives. The structures of all new compounds were established by 1H NMR, 13C NMR and HR MS spectra. The obtained compounds were tested for their cytotoxic properties in cervix carcinoma (HeLa), chronic myelogenous leukemia (K562), acute lymphoblastic leukemia (MOLT-4) and normal endothelial (HUVEC) cells using MTT assay. In these screening studies, we have identified 28 compounds that showed toxicity toward both HeLa, K562 and MOLT-4 cell lines.

Biography

M Napiórkowska, PhD is the Chair of Department of Biochemistry, Medical University of Warsaw. She has been working at the Warsaw Medical University for 18 years. For many years, she has engaged on the synthesis of compounds with biological activity and she is a co-author of 23 publications and two patent applications.

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