

STUDY OF THE INFLUENCE OF A TETRAHYDROISOQUINOLINE BROMINE DERIVATIVE ON FREE RADICAL OXIDATIVE PROCESSES

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Abstract: The development of novel antileukemic agents requires not only high cytotoxic efficacy but also a clear understanding of their underlying mechanisms of action. Oxidative stress-mediated pathways are frequently implicated in cancer cell death; however, alternative mechanisms may offer therapeutic advantages [1].

This study aimed to evaluate the effect of a 1-(2'-Bromo-4',5'-methylenedioxyphenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline derivative, exhibiting high cytotoxicity toward T-lymphoblastic leukemia CCRF-CEM cells, on free radical lipid peroxidation processes in the same cell line.

CCRF-CEM cells were treated with the 1-(2'-Bromo-4',5'-methylenedioxyphenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline derivative at a concentration of 100 μ M. Cytotoxic activity was assessed after 24 h of incubation. The effects on lipid peroxidation were evaluated after 2 h by measuring primary (ketodienes and ketotrienes) and secondary (malondialdehyde) lipid peroxidation products. Cisplatin and dihydroquercetin were used as reference cytostatic and antioxidant compounds, respectively. After 24 h of incubation, the tetrahydroisoquinoline derivative induced complete (100%) cell death in CCRF-CEM cells, whereas cisplatin inhibited cell proliferation by 58.6% and dihydroquercetin by 5.2%. Cisplatin induced a significant increase in ketodiene and ketotriene levels by 27.4% and 61%, respectively, accompanied by a moderate elevation in (MDA) concentration, consistent with previously reported literature data [2]. In contrast, dihydroquercetin reduced all lipid peroxidation markers (malondialdehyde accounted for 51.7%, ketodienes for 41.2%, and ketotrienes for 61.0%). It should be noted that treatment with the 1-(2'-Bromo-4',5'-methylenedioxyphenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline derivative led to a significant reduction in ketodiene, ketotriene, and malondialdehyde levels by 31.8–59.3% compared to the control.

In conclusion, the pronounced cytotoxic effect of the 1-(2'-Bromo-4',5'-methylenedioxyphenyl)-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline derivative in T-lymphoblastic leukemia cells is not associated with the induction of oxidative stress. Its antileukemic activity is likely mediated by alternative biochemical mechanisms independent of free radicals, underscoring the potential of this isoquinoline derivative as a promising candidate for targeted oncology research.

Keywords:

tetrahydroisoquinoline derivative; T-lymphoblastic leukemia; CCRF-CEM cells; cytotoxicity; lipid peroxidation; oxidative stress.

References:

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