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Original Article

THE INFLUENCE OF NITROXYL RADICAL 4-TRIPHENYLPHOSPHONIOACETAMIDO-2,2,6,6-TETRAMETHYLPIPERIDINE-1-OXYL (TPPA-TEMPO) ON GENERAL TOXICITY AND THERAPEUTIC EFFICIENCY OF CYCLOPHOSPHAMIDE ON TRANSPLANTABLE MOUSE LYMPHOSARCOMA LS IN VITRO AND IN VIVO

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ABSTRACT

Systemic administration of nitroxyl radical 4-triphenylphosphonioacetamido-2,2,6,6-tetramethylpiperidine-1-oxyl chloride (TPPA-TEMPO) in subtoxic doses produces moderate inhibitory effect on the growth of mouse lymphosarcoma LS, but does not prolong the lifespan of animals. The latter was due to the light toxic effect of TPPA-TEMPO on animal's visceral organs, especially heart, lungs and kidneys. The administration of TPPA-TEMPO in conjunction with cyclophosphamide (CP) increases anti-tumor therapeutic efficacy which is expressed in both the increase in the life span of tumor bearing animals and in the number of mice cured. However, the values of both effects were not equally dependent on the duration of drug application, presumably, due to the side effects of TPPA-TEMPO on the organisms of the animals. The in vitro studies in the tumor cells cultures have shown that TPPA-TEMPO in small doses decrease metabolism and proliferation rate of tumor cells without affecting cell viability. It was assumed that antitumor effect of TPPA-TEMPO can be associated with either its direct impact on metabolism of tumor cells or the increase in the activity of phagocytes which take part in the mechanisms of antitumor resistance.

KEYWORDS: Nitroxide, Antioxidant, Cyclophosphamide (CP), Mice, Lymphosarcoma LS, Antitumor Activity, in Vitro, in Vivo, Therapeutic Efficacy

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