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ORIGINAL ARTICLE

The cytotoxic effects of some selected gold(III) complexes on 4T1 cells and their role in the prevention of breast tumor growth in BALB/c mice

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Summary

Purpose: *To investigate the cytotoxic activity of newly synthesized gold(III) complexes $[AuCl_2(en)]^+$, $[AuCl_2(SMC)]^+$, $[AuCl_2(DMSO)_2]^+$ (en: ethylenediamine, SMC: S-methyl-L-cysteine and DMSO: for dimethylsulfoxide) in 4T1 mouse breast cancer cell line in vitro and in vivo and to compare their antitumor characteristics with cisplatin complex $[PtCl_2(NH_3)_2]$.*

Methods: *The in vitro, effects of the tested complexes on 4T1 cell viability were determined using MTT colorimetric technique. In vivo, progression of mouse breast tumor growth in BALB/c mice was measured by using external caliper.*

Results: *Among the tested gold(III) complexes, $[AuCl_2(en)]^+$ showed best cytotoxic effects in vitro. The cytotoxic effects of $[AuCl_2(en)]^+$ and $[PtCl_2(NH_3)_2]$ were similar at all concentrations. The data from the in vivo experiment showed that among the tested gold(III) complexes only $[AuCl_2(en)]^+$ can prevent the primary breast tumor growth. $[AuCl_2(en)]^+$ was tolerated well and much better than $[AuCl_2(DMSO)_2]^+$, $[AuCl_2(SMC)]^+$ and $[PtCl_2(NH_3)_2]$ complex which was confirmed by weight gain in mice that received $[AuCl_2(en)]^+$. In addition, mice that received $[AuCl_2(en)]^+$ showed better survival time in comparison with mice that received $[PtCl_2(NH_3)_2]$ complex.*

Conclusion: *$[AuCl_2(en)]^+$ complex seems to be good candidate for future pharmacological evaluation in breast cancer research.*

Key words: cytotoxic effects *in vitro/in vivo*, gold(III) complexes, mouse breast cancer, prevention

Introduction

In preclinical studies it is necessary to test the cytotoxic effects of newly synthesized anticancer drugs *in vitro* and *in vivo* [1]. The use of orthotopic systems gives the most precise information about the capacities of the tested, newly synthesized anticancer drugs to prevent and/or to stop progression of primary tumor growth [2]. In addition, it is of crucial importance to test the newly synthesized therapeutic agents on murine cell lines that will metastasize in a similar manner and to similar locations as the same tumor type will in human.

The human breast cancer is the most prevalent malignancy among women, representing the second cause of cancer-related deaths [3,4]. The 4T1 mammary carcinoma cell line, originally isolated by Fred Miller and coworkers at the Karmanos Cancer Institute [5,6], when introduced orthotopically is useful model for evaluation of primary breast cancer tumor growth progression [7]. In addition, the 4T1 tumor cell line has the capacity to metastasize to all organs affected in human breast cancer, including lungs, liver, brain and bone [8-14].

Although novel molecular pathways relevant to breast cancer biology and breast cancer therapy are explored continuously [15,16], it is expected that a whole array of new agents should be tested in combination or in sequence to standard chemotherapy with the aim to improve the outcome of high-risk breast cancer patients.

The big successes of cisplatin in cancer chemotherapy on one side, and the toxic side effects related to cisplatin treatment on the other side, stimulated the search for new and more selective metal-based anticancer drugs [17].

During the last 20 years, much interest has fo-

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