SUPRESSION OF TUMOUR CELLS GROWTH EXPOSED TO NOVEL VANADIUM COMPLEXES

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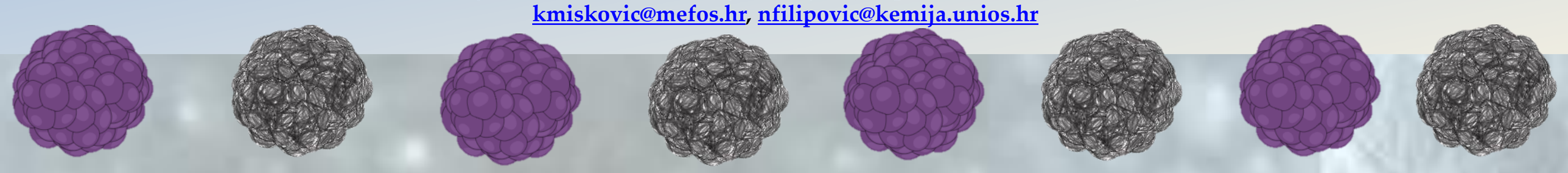

INTRODUCTION

Hydroxypyrones are introduced in the form of complexes with the purpose of achieving the desired concentration of ions in the body and some are used for therapeutic purposes, such as vanadium complexes with proven anti tumour effects. Vanadium complexes exert effects against chemical carcinogenesis on animals, by modifying various xenobiotic enzymes, inhibiting carcinogen-derived active metabolites. Studies on various cell lines reveal that vanadium exerts its antitumor effects through inhibition of cellular tyrosine phosphatases and/or activation of tyrosine phosphorylases.[1] The goal of this research is the preparation of new compounds of vanadium with chromone-2-carboxylic acid and coumalic acid and the examination of their antitumor properties.

MATERIALS AND METHODS

Antiproliferative activity of ligands and vanadium complexes was evaluated by the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (*Fig.1.*)) assay on 7 cell lines obtained from the American Type Culture Collection (ATCC). The malignant cell lines were: Caco-2, HT-29, MDA-MB 231, KATO III, Hep-G2, NCI-H358. The normal cell line was MRC-5 (human fibroblasts). The complexes were dissolved in DMSO at a concentration of 10^{-3} M and applied on cells at final concentrations as follows: 10^{-5} M, 10^{-6} M, 10^{-7} M. All experiments were performed in triplicates.

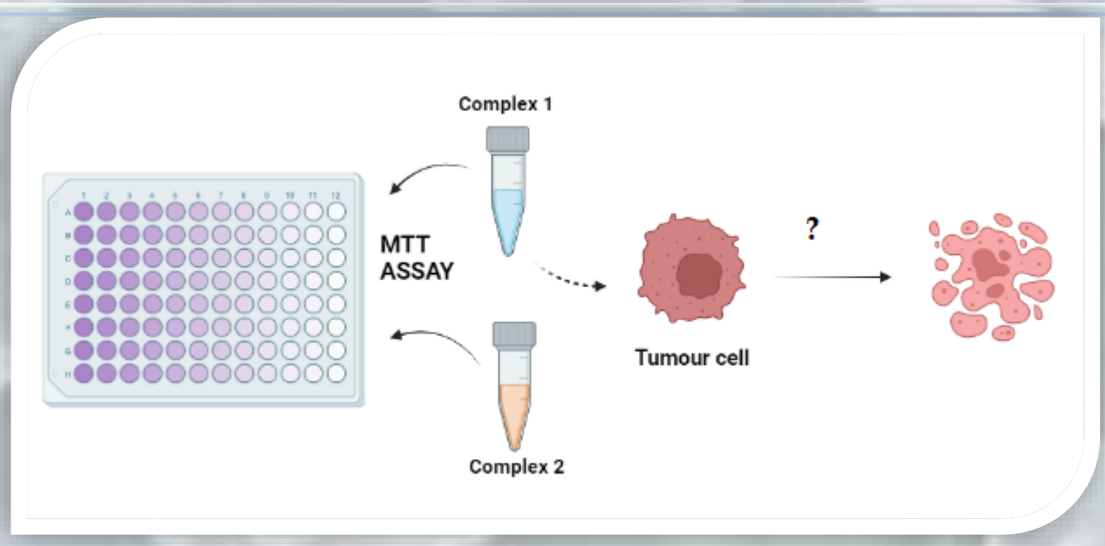

Fig.1. Scheme of MTT assay of vanadium complexes on 2D cell models

RESULTS AND DISCUSSION

Table 1. Antiproliferative activitiy of two vanadium complexes and two complexing ligands at the highest concentration (10^{-5} M)

Cell lines	Complex 1	Complex 2	Ligand 1	Ligand 2
MDA-MB 231	43.4	40.1	98	99.4
Caco - 2	93.9	83.8	89.3	88.9
Hep-G2	66.9	59.4	122.2	118.2
NCI-H358	58.1	58.4	100.9	107.8
KATO III	58.2	51.3	77.1	91.8
HT-29	89.1	86.5	77.3	97.2
MRC-5	54	47	69.7	107.2

Complex 1= $VOSO_4$+ Chromone-2-carboxylic acid
Complex 2= $VOSO_4$+ Coumalic acid
Ligand 1= Coumalic acid
Ligand 2= Chromone-2-carboxylic acid

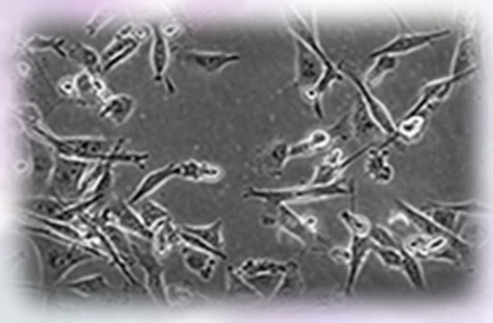

Fig.2. MDA-MB 231 cells

Table 1. shows that the vanadium complexes exhibit selectivity towards breast cancer cells, MDA-MB 231. Unlike the compounds, the ligands did not show antiproliferative activity on any cell line.

MDA-MB-231 (*Fig.2.*) is a highly aggressive, invasive and poorly differentiated triple-negative breast cancer (TNBC) cell line as it lacks estrogen receptor (ER) and progesterone receptor (PR) expression, as well as HER2 (human epidermal growth factor receptor 2) amplification. [2]

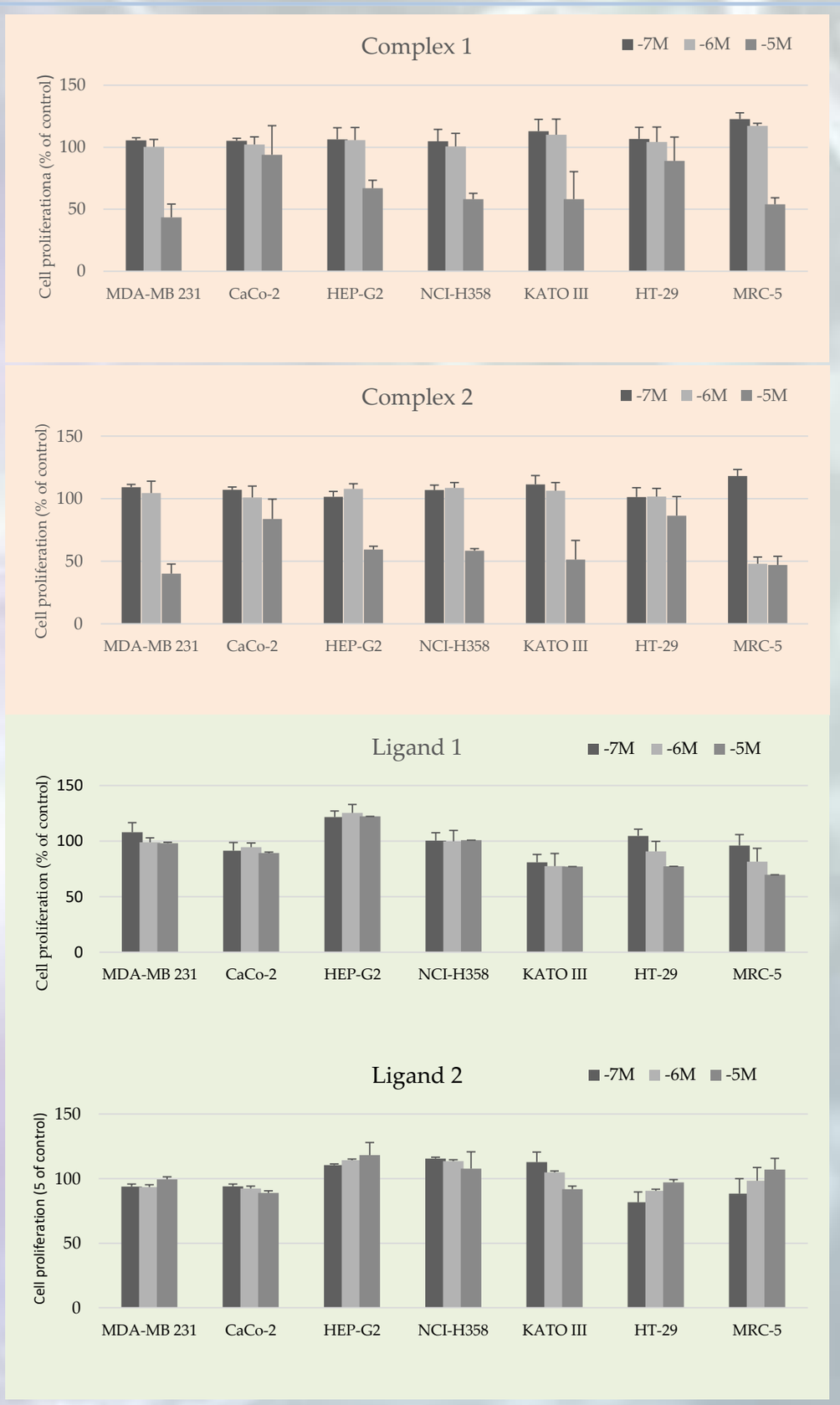

Fig.3. Cytotoxic effect of vanadium complexes and ligands on proliferation profile of 7 cell lines: Data sets are presented as a mean value (X) and standard deviation (±SD) of three independent experiments evaluated by MTT assay

CONCLUSIONS

Based on the obtained results, it can be concluded that the newly synthesized group of vanadium compounds have the potential for future researches of antiproliferative activity on various cancer cell lines with emphasis to breast cancer (MDA-MB 231).

REFERENCES

1. S.Kowalski, D.Wyrzykowski, I.Inkielewicz–Stepniak, Molecular and Cellular Mechanisms of Cytotoxic activity of Vanadium compounds aganist Cancer Cells, *Molecules*, 25, 2020.
2. Cell line profile MDA-MB-231 (ECACC catalogue no. 92020424) (https://www.culturecollections.org.uk/media/133182/mda-mb-231-cell-line-profile.pdf)