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Cu(II) and Zn(II) complexes of salen-type Schiff base ligands as promising anticancer agents in treatment of colorectal adenocarcinoma

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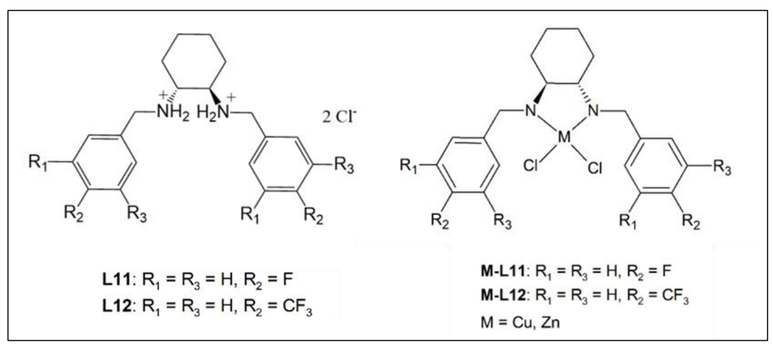
INTRODUCTION & AIM

The study of transition metal complexes and their biological properties (e.g. antimicrobial, cytotoxic, anti-inflammatory, interactions with DNA) are the subject of intensive studies (1). Copper and zinc complexes, as an alternative to platinum-based drugs, display notable anticancer activity while causing fewer side effects than cisplatin. The variation in their biological activity is associated with the molecular structure of the ligand, and the type of central metal ion. Complexes of the salen-type ligands represent a promising group of compounds in medical research.

Since colorectal cancer is the third most diagnosed type of cancer, the aim of this work was to prepare and study the antitumor effect of Schiff base ligands derived from 1,2-cyclohexanediamine and fluorine-substituted benzaldehydes and their Cu(II) and Zn(II) complexes (2,3).

METHODS

- Schiff base ligands were synthesized by condensation of 1,2-cyclohexanediamine and fluorine-substituted benzaldehydes and subsequently reduced with $NaBH_4$.
- Cu(II) and Zn(II) complexes were prepared by the reaction of $CuCl_2$ or $ZnCl_2$ with an equimolar amount of the corresponding Schiff base ligands (Fig.1.).
- Compounds were examined for their cytotoxic activity by MTT assay against human colorectal adenocarcinoma cell lines (HT-29 and Caco-2).



L11: $R_1 = R_3 = H$, $R_2 = F$
L12: $R_1 = R_3 = H$, $R_2 = CF_3$

M-L11: $R_1 = R_3 = H$, $R_2 = F$
M-L12: $R_1 = R_3 = H$, $R_2 = CF_3$

Fig. 1. Structure of Schiff base ligands (L11 and L12) and their Cu(II) and Zn(II) complexes (CuL11, ZnL11, CuL12, ZnL12).

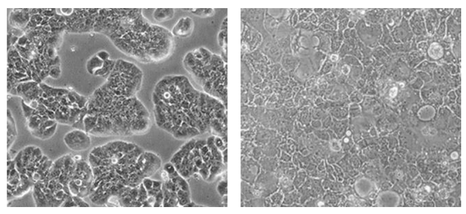


Fig. 2 Human colorectal adenocarcinoma cell lines (HT-29 and Caco-2) tested in MTT assay.

REFERENCES

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RESULTS & DISCUSSION

- Experimental results showed that the studied Cu(II) and Zn(II) complexes significantly decreased the viability of both HT-29 and Caco-2 cancer cells.
- Compounds L12, CuL12 and ZnL12 exhibited stronger cytotoxic activity compared to series 11 (Fig.3).
- Concentration and time-dependent effect on cell viability was observed.

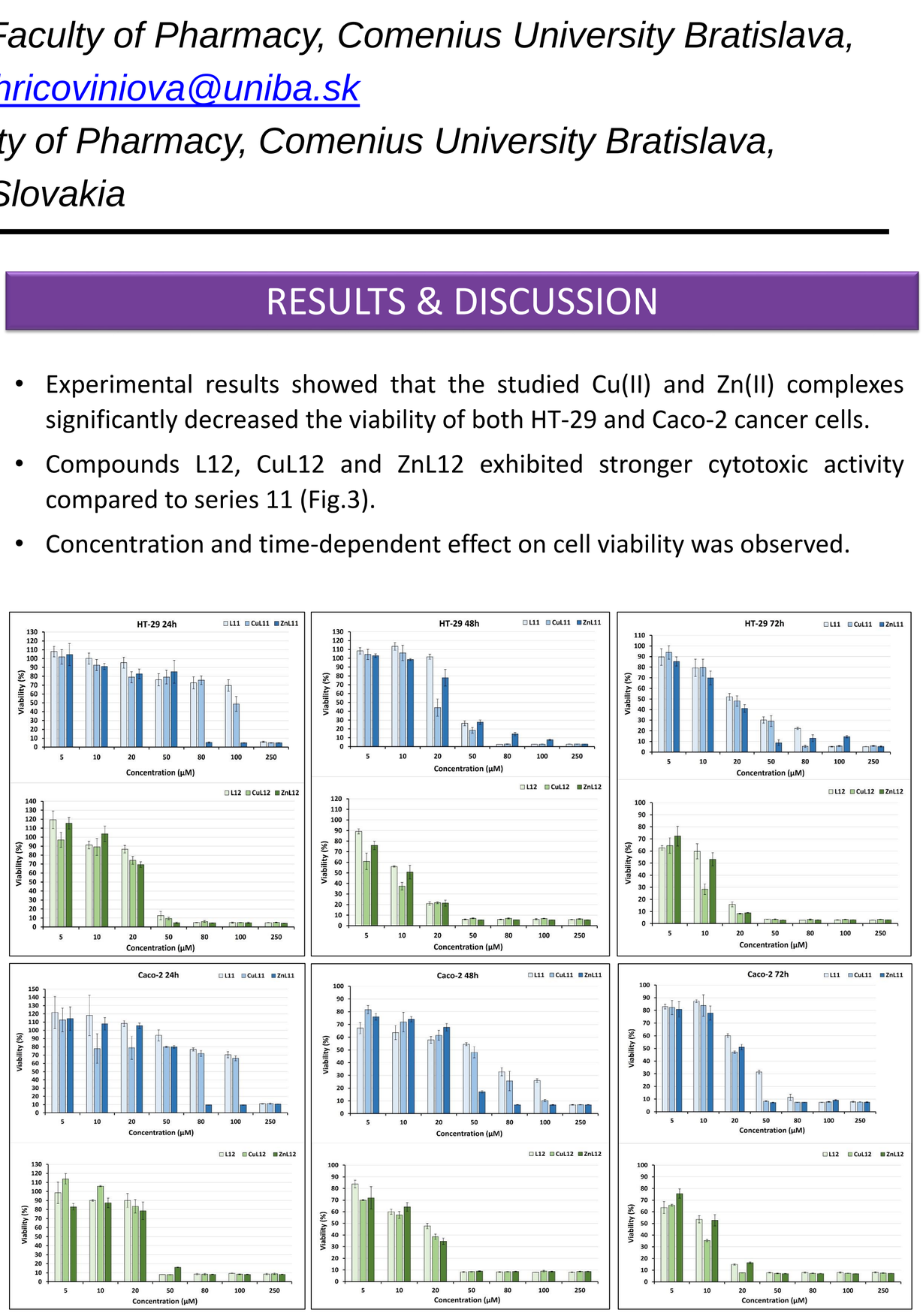

Fig. 3. Experimental results of MTT assay on HT-29 and Caco-2 cell lines after 24h, 48h and 72h treatment. Series of compounds 11 (L11, CuL11 and ZnL11) is shown in blue and series of compounds 12 (L12, CuL12 and ZnL12) is shown in green.

CONCLUSIONS

- **Efficient synthesis of salen-type ligands and their Cu(II) and Zn(II) complexes**
- **Cu(II) and Zn(II) complexes exhibited notable cytotoxic effects against both colorectal cancer cell lines**
- **Compounds L12, CuL12 and ZnL12 showed stronger cytotoxic activity compared to series 11**
- **Due to the marked cytotoxic effect, these metal complexes represent a promising alternative for the development of new anticancer agents**

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