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ABSTRACT BOOK

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centrations of ITF3756 and BTZ markedly reduced HCT116 cell viability when used in combination. The two compounds together also promoted lipid accumulation as evidenced by red-oil staining. These effects were associated with a marked decrease in the levels of the full length SREBP protein and increase in PPARg, both events correlated with lipogenesis. Ongoing studies aim to clarify the molecular mechanism of cell death induced by the combination ITF3756 and BTZ and the extent of lipid involvement in these events. Overall, these preliminary results suggest that inhibiting HDAC6 and the proteasome may represent a key strategy to target colon cancer unbalancing lipid metabolism.

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REFERENCES

1. Zhang SL *et al.* Onco Targets Ther. 2019; 2;12:2409-2419. doi: 10.2147/OTT.S194986.
2. Qian H *et al.* J. Clin. Invest. 2017 3;127(4):1353-1369 doi: 10.1172/JCI85963.
3. Xu G *et al.* Br J Pharmacol. 2021; 178(23):4741-4757. doi: 10.1111/bph.15653.

CYTOTOXIC EFFECT OF A NOVEL METAL SCHIFF BASE COMPLEX ON HEPG2 HUMAN TUMOR CELLS

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Metal-based compounds show numerous applications in the field of medicine and among these their anticancer effects stand out. Most of the latter are likely due to their binding with DNA, even in the form of non-canonical folding, such as guanine-quadruplexes[1,2]. In this scenario, three Ni(II), Cu(II), Zn(II) complexes of a salphen-like N4-donor ligand were synthesized and their potential cytotoxic effects on HepG2 human hepatocarcinoma cells investigated. First, interesting data emerged from cell viability studies which showed that among the compounds, only the Cu(II) complex exerted a markedly dose-dependent cytotoxic effect at 24 h *vs.* control. Moreover, no significant viability-restraining effect was exerted by either the sole scaffold at all the concentrations tested, or Cu(II) acetate except for the maximum concentration assayed (100 □M). The IC_{50} value at 24 h of the Cu(II) complex was determined and the IC_{50}-treated cells were submitted to a panel of analyses aimed to the evaluation of the biological aspects of cytotoxicity, as reported[3,4]. First, staining with propidium iodide for cell cycle analysis showed the accumulation of treated HepG2 cells in the sub-G_0G_1 fraction without perturbations of the morphological appearance and cell cycle profile, thereby suggesting the occurrence of a higher level of DNA fragmentation, which is associated with cell death. Staining with annexin V-FITC and PI indicated that after exposure the percentage of the viable annexin V^-/PI^- cells decreased from about 88% of the controls to about 59% and, on the other hand, the percentage of the apoptotic annexin V^+/PI^+ cells increased from about 6% of the controls to about 35%. The activity of the caspase proteases possibly involved in the cytotoxic effect was tested and the results obtained showed the activation of caspase-3, executor of classical apoptosis, and -5, an inflammatory caspase known to interact with caspase-3 and induce pyroptotic cell death[5]. Interestingly, the increase of the proteolytic cleavage of GSDME protein, a key event in pyroptosis activation, was detected through Western blot. Further, we investigated whether cell exposure could impair the mitochondrial function and cell redox status, demonstrating that the Cu(II) complex induced the dissipation of the mitochondrial membrane potential and the up-regulation of ROS. The preliminary data obtained represent a valuable starting point for the study of the biological mechanisms underlying the potential beneficial effect of the Cu(II) complex on liver tumor cells, so far tested only *in vitro*, and further studies will be necessary to better define the intracellular pathways targeted by this cytotoxic molecule.

REFERENCES

1. Farine G, *et al.*, Eur J Inorg Chem 2021;1332-1336.
2. Lauria A, *et al.*, Dalton Trans 2014; 28:6108-6119.
3. Abruscato G, *et al.*, Biology, 2023; 12:616.
4. Luparello C, *et al.*, EXCLI J, 2022; 21:722-743.
5. Wu Y, *et al.*, J Cell Physiol, 2019; 234:13571-13581.

NOVEL ULTRASTRUCTURAL INSIGHTS INTO CLEAR CELL CARCINOMA OF THE PANCREAS: A CASE REPORT

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Clear cell primary adenocarcinoma of the pancreas (CCCP) is a rare histological subtype of pancreatic ductal adenocarcinoma (PDAC), still poorly characterized (1, 2). We reported a case of CCCP in a 65-year-old male with the aim to dissect the complexity of this morphological variant by means of molecular and ultrastructural investigations. Molecular genetic testing did not detect any mutational variants for BRCA1 and BRCA2.Immunohistochemical staining with Mucicarmine and Alcian-Pas demonstrated that the clear-cell foamy appearance was not due to a hyperproduction of mucins. Ultrastructural characterization revealed the massive presence of mitochondria in the clear cell cytoplasm. Mitochondria showed disrupted cristae and various degrees of impairment of structural integrity. To evaluate the functional state of mitochondria, immunohistochemistry staining for NADH dehydrogenase [ubiquinone] 1 alpha subcomplex, 4-like 2 (NDUFA4L2), a subunit of Complex I of the mitochondrial respiratory chain which transfers electrons from NADH to ubiquinone, was carried out. Interestingly, while the clear cells were NDUFA4L2 negative, ductal adenocarcinoma areas proved positive to the stain, suggesting a different functional state of mitochondria. Thus, our ultrastructural