IN SILICO RESEARCH, ANTITUMOR AND ANTIOXIDANT ACTIVITY OF CHELATE COMPLEXES CONTAINING NI (II)

Guermaz F., Suleiman M.M., Kobzar N.P., Grinevich L.O., Perekhoda L.O.
The National University of Pharmacy, Kharkiv, Ukraine

Introduction. The chemistry of Schif bases has been discussed extensively over the past few decades due to their broad range of biological, biochemical and pharmacological activities. It is a commonly used organic ligand having –C=N– linkage and can coordinate to different metal ions via azomethine nitrogen. The activity is enhanced when these compounds are forming complexes with various metal ions. Most of the divalent transition metal ions have an important role in the biological processes in the human body. The study of their coordination chemistry with mixed ligands has been one of the important developments in the feld of bioinorganic chemistry. Over the years, ternary complexes, often referred as mixed ligand complexes have received considerable attention due to their wide role in analytical chemistry. However, recent studies showed that the ternary complexes with biologically potential ligands fnd use in various enzymatic reactions and a large number of biological studies.

Aim. *In silico* research, antitumor and antioxidant activity of chelate complexes containing Ni (II)

Materials and methods. The human colon carcinoma (HCT-116), human hepatocellular liver carcinoma (HEPG-2) and human breast carcinoma (MCF-7) cell lines were used for this study. These cell lines were obtained in the frozen state under liquid nitrogen (-180 °C) and maintained by serial sub-culturing in National Cancer Institute, Cairo University, Egypt. The antioxidant activity of these studied chelates was determined at RCMB, Al-Azhar University by DPPH free radical scavenging assay. The reported compounds were optimized and examined by Gauss View 6.0.16 graphical interface program.

Results and discussion. To understand the complexation reaction and discover the reactive site in a conjugate system FMO's studies play important roles. The molecular energies of E_{HOMO} and E_{LUMO} for the main ligand and all of its nickel complexes apparently explain the global reactivity descriptors such as chemical potential, chemical hardness and electrophilicity. Such analyses are helpful to describe the chemical reactivity of the compound and the identification of the reactive sites in the molecular system. The energy difference between the highest occupied molecular orbital's and lowest unoccupied molecular orbital's level clearly explaining the charge-transfer interaction. The two important quantum chemical parameters as global hardness and global softness predicted

from the band energy between HOMO–LUMO orbitals i.e. hard molecule large band gap and soft molecule small band gap. If we compare the chemical softness of the ligand is less than all Ni(II) complexes, therefore, the reactivity of the ligand greater than all complex. Further some key parameter, such as the electrophilicity assign a positive value, which quantifes the tendency of the system to accept an electron from the surrounding that clearly explains the complexes are more stable than the free ligand.

The in vitro growth inhibitory activity of the prepared ternary Ni (II) complexes was evaluated against HCT-116, HEPG-2 and MCF-7 cell lines along with the standard anticancer drug doxorubicin to assess cell proliferation. The IC50 values of the tested compounds were determined and compared with doxorubicin. We know, the compounds exhibited IC50 value below 5.00 μg/ml, within the range of 5.00–10.00 μg/ml and 10.00–25.00 μg/ml are considered strong, moderate and weak anticancer agents, respectively. The obtained data showed that compounds were found to be more potent against all cancer cell lines.

The scavenging ability determines the antiradical power of an antioxidant. Here, the free radical scavenging activity evaluation is carried out to determine the antioxidant activity of all the tested ternary Ni (II) complexes at 5, 10, 20, 40, 80, 160, 320 and 640 μg concentrations by measuring the decrease in the absorbance of DPPH at 517 nm. Ascorbic acid is used as a standard drug. The results of DPPH radical scavenging analysis displayed the dose–response curve of DPPH radical scavenging activity of ternary Ni(II) complexes compared with ascorbic acid. It was observed that at the lowest concentration (5 μg), the antioxidant activity of ascorbic acid was found to be 12.98%, but this value is increased to 14.71% for tested complexes. Meanwhile, this percentage is decreased in the range of 9.58- 10.19% `in the other mixed ligand complexes.

Conclusion. The anticancer and antioxidant properties of some ternary nickel complexes have been reported. The Schif base acts as a primary ligand (HL1) whereas; anthranilic acid (HL2), 2-nitroaniline (HL3), alanine (HL4) and histidine (HL5) act as secondary ligand or co-ligand. The anticancer activity of these compounds was studied against human colon carcinoma (HCT-116), human hepatocellular liver carcinoma (HEPG-2) and human breast carcinoma (MCF-7) cell lines. The obtained data showed that compounds were found to be more potent against all cancer cell lines. The antioxidant activity of these compounds was evaluated using DPPH radical scavenging and compared with ascorbic acid. The DFT computations for these compounds were made to understand the mode of bonding. The molecular orbital energy gap between HOMO and LUMO for complexes are established to be less than source ligand.