NEW PLATINUM(II) COMPLEXES WITH MODIFIED TRIAZOLE AND IMIDAZOLE LIGANDS AS POTENTIAL ANTICANCER AGENTS

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Cancer is a global health problem and is the second leading cause of death after cardiovascular disease. Currently, the most widely used treatment is chemotherapy. However, the atypical structure of cancerous tumors and the development of numerous defense mechanisms by cancer cells cause an effective anticancer drug that has not been discovered yet. Therefore this research area is still extensively developed. A promising group of design coordination compounds with anticancer properties is heteroaromatic compounds. Numerous benzofuran derivatives such as piperazine-based benzofuran derivatives, 2-aminobenzofuran derivatives, dihydrobenzofuran derivatives [1] exhibit anticancer activity both *in vitro* and *in vivo*. Similarly, N-heterocyclic compounds based on triazole [2] or imidazole[3] moiety have greater anticancer activity than commercially available anticancer drugs.

Bearing in mind the above literature reports, we decided to combine benzofuryl α-azole ketones with platinum(II) ion to take advantage of the potential anti-cancer effect of benzofuran and azole groups on the one hand, as well as the known therapeutic potential of platinum(II) complexes.

Four new square-planar platinum(II) complex compounds with general formulas *cis*-[$Pt(bfte)_2Cl_2$] (1), *cis*-[$PtCl_2(bfie)_2$] (2), *cis*-[$PtCl_2$(bfte)(dmso)] (3), *cis*-[$PtCl_2$(bfte)(dmso)] (4) where bfte - 1-(benzofuran-2-yl)-2-(1H-1,2,4-triazol-1-yl)ethenone, bfie - -(benzofuran-2-yl)-2-(1H-imidazol-1-yl)ethenone, dmso - dimethyl sulfoxide was obtained. Based on ^{1}H, ^{13}C, ^{15}N, ^{195}Pt NMR, and IR analyses, it was confirmed that in complexes (1) and (2), the platinum(II) ion is bound monodentate two N-donor ligands (Δcoor. ^{15}N NMR=94.2 - 102.2 ppm), while in complexes (3) and (4) the platinum(II) ion is bound to one monodentate coordinated N-donor ligand (Δcoor. ^{15}N NMR=79.9 - 89.3 ppm) and S-donor dimethylsulfoxide molecule. Two chloride ions complement the coordination sphere of all four complexes in the *cis* position.

Preliminary *in vitro* studies have shown that complex (1) at a concentration of 10 μM reduces the viability of bladder cancer cell lines T24 and CRL1472 by approximately 85% and 75%, respectively. In contrast, cisplatin at the same concentration reduces cell viability by 25% and 15%, respectively. Additionally, all four newly obtained coordination platinum(II) compounds show a lower affinity towards glutathione than cisplatin. Thus there is a possibility that they can more effectively avoid the mechanism of drug resistance associated with binding to this tripeptide.

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[1] A.A. Abbas, K.M. Dawood, RSC Adv. 13 (2023) 11096–11120.

[2] M.M. Alam, Archiv Der Pharmazie 355 (2021) 2100158.

[3] I. Ali, M.N. Lone, H.Y. Aboul-Enein, Med. Chem. Commun. 8 (2017) 1742–1773