Improving anticancer activity, stability, and lipophilicity of cisplatin ~~by~~ through substitution of different amine ligands

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In this study, several cisplatin analogs were designed to investigate the antitumor activity and lipophilicity effects ~~with~~ in amine change. The amines of the cisplatin molecule were substituted with aliphatic amines in different analogs. The ~~C~~cytotoxicity of analogs against human colon cancer (HCT116) was investigated using MTT assay and spectroscopic methods were used to determine the DNA binding mode. Cytotoxicity studies revealed cisplatin and *cis*-dichloro-diisobutylamine-platin ~~are~~ were strong and weak inhibitors of human colon cancer cells (HCT116), respectively. DNA denaturation study ~~represents~~ indicated that the stability of DNA in the presence of these compounds ~~decreases~~ diminished and substitution of propylamine and methylamine groups increased DNA denaturation. ~~Moreover~~Further, the interaction of the desired compounds with DNA ~~is~~ proved to be a spontaneous process**.** Tm analysis also ~~reveals~~ revealed that cisplatin, *cis*-dichloro-dimethylamine-platinum, and *cis*-dichloro-dipropylamine-platinum complexes ~~make~~ made DNA double helix unstable via covalent bond, while *cis*-dichloro-dibutylamine-platinum and *cis*-dichloro-diisobutylamine-platinum stabilized DNA via electrostatic binding to DNA. The ~~R~~results of fluorescence studies ~~reveal~~ showed that the quenching nature of cisplatin, methyl-, and propyl- systems ~~are~~ was dynamic while the static quenching ~~is~~ was observed in the presence of *cis*-dichloro-dibutylamine-platinum and cis-dichloro-diisobutylamine-platinum. The molecular docking simulations and DFT analysis were performed to investigate the binding sites and chemical behavior of cisplatin analogs, respectively. Molecular docking ~~showed~~ demonstrated that except *cis*-dichloro-diisobutylamine-platin, other complexes ~~have~~ had higher negative docking energy than cisplatin for interaction with DNA, and methyl and propyl complexes may be good candidates for ~~the~~ anticancer drugs.