

1.15 pmThe synthesis of platinum (II) – nuclear localization sequence peptide hybrid for nanoparticle<br/>development and anticancer therapy.

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Platinum (II) therapy is a well-established treatment of many malignancies, including ovarian cancer, and cisplatin is one of the most potent therapeutics. Fast aquation rate of cisplatin leads to its high systemic toxicity, which led to development other platinum based agents like carboplatin, with better toxicity profiles but lower effectiveness. Our work comprises the synthesis of new carboplatin-like Pt (II) complexes  $C_{10}H_{21}N_5O_4Pt$  and  $C_{10}H_{18}N_2O_4Pt$ , with azide and alkyl functionalities that can be attached onto other supports to facilitate drug delivery. We formed Pt (II) peptide hybrid with SV40 large T antigen derived PKKKRKV peptide. The peptide used belongs to the nuclear localization sequence (NLS) that comprises the intrinsic cellular machinery of nuclear transport and was used to amplify the Pt (II) entry into the nucleus. The hybrid is highly soluble in water (<50 mg/ml), compared to cisplatin (2.5 mg/ml) and carboplatin (10 mg/ml). We found that Pt-NLS is highly efficacious in vitro, lowering the viability better than carboplatin in chemo naïve and in chemo resistant cancer cell lines. The methodology can be extended further to incorporate the Pt (II) complexes into polymeric nanoparticles.