

## 2<sup>nd</sup> International Summit on **Clinical Pharmacy**

December 02-03, 2014 DoubleTree by Hilton Hotel San Francisco Airport, USA

### Polymer conjugates of platinum(II) complexes

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Macromolecular conjugates of platinum(II) complexes have been designed and evaluated *in vitro* as drug delivery systems. The polymer component has multiple functions – through conjugation to decrease the toxicity of the bioactive complex, to protect it against binding and degradation by plasma proteins, to prolong blood circulation and to assist the passive drug targeting. On engineering the conjugates, the choice of the polymer carrier was also consistent with the functionality and structure of the platinum complex and the possibility to obtain stable nanocolloidal aqueous solutions.

The dinuclear platinum complex with a spermidine bridge was attached to poly(oxyethylene H-phosphonate)s via a phosphoramidate bond. <sup>1</sup>H and <sup>31</sup>P{H} DOSY NMR spectral data proved the conjugation reaction. The new species had an average size from 10 nm to 24 nm depending on the molecular mass of the polyphosphoester chain. The conjugates exhibited profound cytotoxicity in a panel of five chemosensitive human tumor cell lines and one cisplatin-resistant model (HL-60/CDDP), and were found to induce apoptotic cell death.

Core-shell type star polymer bearing carboxylate functions was used as nanocarrier of cisplatin. The stars were loaded with cisplatin achieving remarkable high drug payload of 45% (w/w). The conjugates displayed sustained manner of Pt(II) complex release without initial burst effect. *In vitro* cell viability study, using four human tumor cell lines proved that the conjugates exhibited lower cytotoxicity compared to the free agent. The established cellular accumulation of cisplatin indicated uptake of the nanoconjugates by the cells through endocytosis. A feasible PEGylation procedure of the carrier was proposed using the drug as a reversible linker for PEG modification of the star macromolecules.

### Biography

Neli Stoyanova Koseva has completed her PhD in 1994 from Sofia University and postdoctoral studies from UCL School of Pharmacy, UK. Presently, she is the director of the Institute of Polymers at the Bulgarian Academy of Sciences, Sofia, Bulgaria. She has been coordinator of nationally and EU funded projects. She has published more than 25 papers in reputed journals.

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