



Revolutionizing Sunitinib Malate: Metal Complex-Loaded Polymeric Nanoparticles for Enhanced Targeting of Tyrosine Kinase Receptors in Renal Cell Carcinoma Treatment

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Abstract

Sunitinib malate, an oral multikinase inhibitor used for treating renal cell carcinoma, exhibits characteristics of a high-solubility compound with limited absorption (Class III). With pharmacokinetics indicating low bioavailability, an extended elimination half-life (40 to 60 hours), and predominant excretion through feces (60%) and kidneys (16%), there is a need to enhance its cancer-targeting efficacy. This study focuses on improving Sunitinib Malate's targeting ability to Tyrosine Kinase receptors by formulating it into metal complex-loaded polymeric nanoparticles. Chitosan and PEG polymers are employed for this purpose. In-depth in silico studies compare Sunitinib's binding affinity with different bivalent metals (Cu, Zn, Fe). The formulation of Sunitinib-Copper complex loaded polymeric nanoparticles is achieved by solvent evaporation method. Key assessments include particle size, zeta potential, PDI, entrapment efficiency, drug content, in vitro drug release, and MTT assay for cell viability against A498 (Renal cell carcinoma). The Sunitinib-Cu complex demonstrates superior binding affinity (-7.5) compared to other metal complexes. The resulting copper nanoparticle-loaded with chitosan and PEG polymer exhibits a particle size ranging from 9 to 300 nm, with zeta potentials of (-14 to -33) mV for PEG NP and (14 to 33) mV for chitosan NP. Entrapment efficiency is over 83%, and in vitro drug release surpasses 85%. MTT assay results indicate a cell viability of 23.88% after 24 hours at a concentration of 5 µg/ml for SM-Cu chitosan NPs, outperforming SM-Cu complex-loaded PEG NP (29.39%). These findings suggest that Sunitinib-Cu complex-loaded polymeric nanoparticles, prepared through solvent evaporation, present a promising carrier to enhance efficacy at Tyrosine Kinase receptors.

Keywords

Sunitinib malate, Nanoparticle, Chitosan, PEG, Copper Complex, MTT Assay.