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DNA binding of Sunitinib: spectroscopic evidence via circular dichroism and nuclear magnetic resonance

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Highlights

- Plasmid DNA can be used in DNA-ligand binding experiments with certain considerations.
- A two-step binding mechanism is proposed for sunitinib.
- In the first step, the superhelix unwinds and in the second step additional ligands bind to the DNA.

Abstract

Sunitinib is a non-selective tyrosine kinase inhibitor, but in its chemical structure there can be discovered certain features, which suggest the ability to bind to DNA. These elements are the planar aromatic system and the tertiary amine function, which is protonated at the pH of the organism. In this study, the binding of the drug sunitinib to DNA was investigated using circular dichroism (CD), ¹H NMR and UV spectroscopies, along with CD melting. For these studies DNA was isolated from calf thymus (CT), salmon fish sperm (SS), and chicken erythrocyte (CE), however for our purposes an artificially constructed and highly purified plasmid DNA (pUC18) preparation proved to be the most suitable.

DNA binding of the drug was confirmed by shifts in the characteristic CD bands of the DNA, the appearance of an induced CD (ICD) signal in the upper absorption region of sunitinib (300 nm – 500 nm), and the evidence from CD melting studies and the NMR. Based on the CD and NMR measurements, it can be assumed that sunitinib has a multiple-step binding mechanism.

Keywords: Sunitinib, Circular Dichroism, Induced Circular Dichroism, ¹H NMR, Saturation transfer, DNA

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