Abstract

Sunitinib and vandetanib are anti-cancer medications prescribed for medullary thyroid cancer (in the case of vandetanib) and for renal cell carcinoma, gastrointestinal stromal tumor, and pancreatic cancer (in the case of sunitinib). They belong to the group of tyrosine kinase inhibitors and act by exhibiting anti-angiogenic effects and by inhibiting tumor cell proliferation and survival through VEGFR. Additionally, vandetanib also inhibits tumor cell survival via EGFR and RET.

In the presented thesis, we investigated the binding interaction between serum albumin and the TKIs vandetanib and sunitinib using BSA, HSA, and blood plasma. We examined the differences in interaction between the TKIs and various serum albumins, including pure BSA, pure HSA, and blood plasma, as well as the nature and location of the binding interaction. Additionally, we studied the influence of other ligands on this interaction and the photosensitivity of sunitinib itself.

Utilizing spectroscopic techniques, including UV-VIS absorption and fluorescence quenching, we have determined the Stern-Volmer and binding constants, as well as the thermodynamic parameters, for the binding interactions of sunitinib and vandetanib with BSA and HSA. Our results indicate that complex formation occurs between BSA and sunitinib, BSA and vandetanib, HSA and sunitinib, and HSA and vandetanib, as demonstrated by both the fluorescence quenching and UV-VIS absorption data. The high binding constants of sunitinib and vandetanib demonstrate a substantial affinity to serum albumin, which allows for effective drug transport to the intended site via the bloodstream. The strong binding affinity was further confirmed by utilizing centrifugation filters during HPLC analysis. Based on the thermodynamic parameters, both TKIs primarily interact with HSA and BSA through hydrophobic interactions. Fluorescence quenching data in the presence of Sudlow binding site I and II markers revealed the binding site of sunitinib and vandetanib to BSA in subdomain IIA (Sudlow site I). The formation of ternary complexes of sunitinib, vandetanib and BSA was also demonstrated, and a significant effect of ions on the binding interaction of sunitinib and vandetanib with BSA was observed. Using the HPLC method, it was determined that the maximum degradation of Z-sunitinib occurs during the first twenty minutes of exposure of the sample to light.

Key words: tyrosin kinase inhibitors, sunitinib, vandetanib, serum albumin, HPLC, spectroscopic methods