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Preparation and studies on complexes and conjugates of silsesquioxane with anthracyclines

SUMMARY

Anthracyclines are widely used in modern chemotherapy in the form of their hydrochlorides. Anthracyclines intercalate into DNA helix, leading to inhibition of tumor cell division and their apoptosis. Unfortunately, their application is limited due to side effects, i.e. myocardial damage and infarction associated with taking a high dose of drugs in an uncontrolled manner.

The solution to the problem offered by contemporary biomedicine is the coupling, physical adsorption or complex formation of anthracyclines with appropriate carriers. The use of POSSs (polyhedral silsesquioxanes) with anticancer drugs allows controlled transport of anthracyclines to cancer cells. An important feature of POSS derivatives is their biodegradability, biocompatibility, nanometer size and lack of toxicity. In addition, due to the possibility of their functionalization and the presence of eight corners, they allow to attach various drugs at the same time.

In this doctoral dissertation I presented the synthesis of POSS organosilicon carriers containing amino groups in the form of hydrochloride and carboxyl groups as a result of the thiol-ene reaction. The first type was used for conjugation with previously modified daunorubicin to form an amide bond or to form complexes with doxorubicin exploiting non-covalent bonding. The second POSS with COOH functions was conjugated with doxorubicin to also form amide bonds. In the dissertation I presented modifications of anticancer drugs (doxorubicin and daunorubicin) as compounds required for conjugation with nanocarriers. I also identified the character of non-covalent interactions between aminopropyl silsesquioxane and doxorubicin. The obtained results confirmed that such complex acted more effectively than the pure drug itself.

The obtained results were confirmed by the following tests and analyzes: NMR spectroscopy (^{1}H NMR, ^{13}C NMR, HSQC, COSY, NOESY), FTIR, fluorescence spectrometry, elemental analysis, MALDI-TOF mass spectrometry, ESI MS, DLS and Z-potential.

These studies on complexes and their enhanced efficacy point to the importance of such the systems in development of novel prodrugs without often complicated syntheses. Going a little bit further one may predict that POSSes with other functional groups can be effective carriers for much wider range of anticancer drugs.

It can be expected that my research and synthesis of new nanoconigates and nanocomplexes of anthracyclines with POSS will significantly broaden the knowledge about the possibilities of synthesis of prodrugs and effectiveness of chemotherapy, although this will require further studies by pharmacological and medical centers.