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# Synthesis of complexes based on platinum

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Main aim of this study was the revision of the synthetic methods of cisplatin, or cis-diamminedichloroplatinum(II) with an outlook to the preparation of 195mPt-labelled complex. [1]
Historically it was the first member of platinum-containing cytostatic drug. Nowadays carboplatin and oxaliplatin are also being used as the non-specific anticancer drugs. Cisplatin reacts with nitrogen in purine and pyrimidine bases of DNA molecule, what causes the inhibition of cell division and leads to apoptosis. Cisplatin is used widely especially in the combination with other drugs in the treatment of testicular cancer, ovaria cancer, bladder cancer, breast cancer, osteosarcoma etc. Since cisplatin acts non-specifically its use is universal, however it has several drawbacks and side effects such as nephrotoxicity and sickness. [1]
Chemically cisplatin is not very stable compound. It is less stable than carboplatin and hydrolyzes in aqueous solutions. This can be inhibited by adding excess chloride ions. Also transformation from cis to trans isomer is possible due to light sensitivity. The trans isomer has mutagenic properties. [1-4]
Several articles with detailed synthesis description were found. There are two methods of synthesis and both methods were examined. However only one of them was successful. In the future this method will be used in synthesis of cisplatin and other platinum complexes with radioactive Pt-195m, which can increase cancer toxicity of studied drugs. [2-5]
The key step in the synthesis of all platinum complexes is the reduction of Pt(IV) to Pt(II), which can be made e.g. with hydrazine in aqueous solution of chloroplatinic acid (H2PtCl6) [2-4]. Main reactant for following reactions is potassium tertachloroplatinate (K2PtCl4) obtained after reduction. Based on this compound any other platinum complexes can be easily prepared. For cisplatin synthesis ammonia solution was used. Difference between two methods is in substitution step. To increase the yield of the cis isomer chloride ion can be replaced by iodide. Next step is to substitute iodide ions with ammonia. After that iodide should be replaced by chloride by adding silver nitrate. Silver iodide precipitate can however cause contamination of the product. [2,4]
Another method eliminates the step with chloride replacement, but cis and trans isomers are obtained after adding of ammonia solution. This isomers can be successfully separated, because of different solubility of cis and trans isomers in 0.1M hydrochloric acid.[3]
The second method for synthesis was successful. Structure analysis of obtained product was performed by MS spectrometry. Yields of this synthesis was not satisfactory, mainly because of problematic reduction of Pt(IV). Platinum(II) is unstable compared to metallic platinum and platinum(IV). The reduction step is being optimized. Obtained yield was 35%, what is smaller than published results of 43% [2], 95% [3] and 50% [4], but the work was made with micro amounts of platinum (about 20 mg), what made synthesis more complicated.

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