SURFACE MODIFICATION OF CARDIAC STENTS USING NEW COORDINATION COMPOUNDS WITH POTENTIAL ANTITHROMBOGENIC PROPERTIES

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Introduction

The safety and efficacy of percutaneous coronary intervention have improved significantly over the past 40 years. In particular, the introduction of a drug eluting stent (DES) was an important breakthrough in interventional cardiology [1,2]. Currently, newer and newer drug-eluting stents are appearing and further clinical trials are being conducted to assess their efficacy and safety [3]. The disadvantage of DES stents is the increased likelihood of late thrombosis on compared to BMS. This is due to the fact that DES release antiemotic drugs (sirolimus, paclitaxel, everolimus or zotarolimus), which delay the endothelium of the stent surfaces. Patients requiring DES implantation must therefore receive PCI antiplatelet therapy. [4,5]. Drug-eluting stents (DES) have three components: a metallic stent platform, a polymer coating, and a medicinal agent (FIG. 1) [6,7]. Polymer coatings that are applied to the surface of the stent serve as drug carriers and allow controlled drug release. Advances in polymer technology aim to reduce local inflammatory reactions and thrombosis by improving the biocompatibility of polymers. Currently, biodegradable polymers are being introduced, and during their decomposition, the drug is gradually released [7]. Our research will concern the modification of stent surfaces with a bioresorbable polymer, which will gradually release the anticoagulant drug.

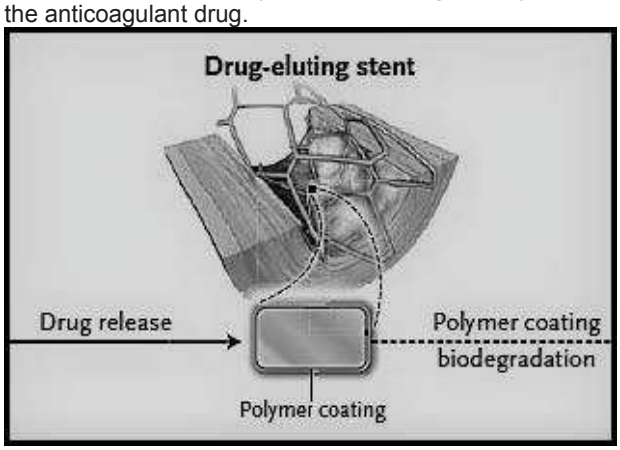

FIG. 1. Construction of drug-eluting stents [5].

Materials and Methods

A key point in our research is the synthesis of coordination compounds with the desired antithrombogenic properties. New coordination compounds were obtained through the synthesis of titanium(IV) alkoxides with substance possesing anticoagulant properties (acetylsalicylic acid (ASA)). It is also planned to obtain titanium (IV)oxo-complexes with other anticoagulants such as warfarin, clopidogrel and heparin.

The reaction of Ti(IV) alkoxides with acetylsalicylic acid was carried out in a 4:1 molar ratio. For this purpose, 0.16 g of ASA was dissolved in 1 ml of a solvent (THF/ BuiOH (1:1), THF/PriOH (1:1)) and added to 1 ml of titanium (IV)isopropoxide or 1.19 g of titanium(IV) isobutoxide, in room tempaerature, under Ar.

Results and Discussion

The obtained results of the synthesis of titanium (IV) oxo-complexes with acetylsalicylic acid seem to be promising. We managed to obtain a crystalline form necessary for detailed structural studies of the compounds obtained.
Reactions conducted with titanium (IV)isobutoxide seem to give better results than using titanium(IV) isopropoxide. Out of the various solvents tested, the 1: 1 mixture of THF with BuiOH seems to be the best.

Conclusions

The conducted research proved that it is possible to synthesize titanium (IV)oxo-complexes with such anticoagulant, as ASA, using the method proposed by our team. Further studies will be carried out with the use of other anticoagulants (warfarin, heparin, clopidogrel). Studies show [8] that combination therapy and dual antiplatelet therapy with aspirin and clopidogrel and warfarin are also possible. This knowledge can also be an inspiration for our further research.

Acknowledgments

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