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Final Report

for 1 month work in the AG Prof. Erckart Ruehl
at Institute of Chemistry and Biochemistry
Frei Universität Berlin

My visit to the Institute of Chemistry and Biochemistry FUB as funded by DAAD had two general purposes: scientific and organizational ones. The scientific part was devoted to the research of new nanocarriers for transdermal drug delivery. The organizational work included the finding out of collaboration points as well as taking an experience of research management in FUB.

An important prerequisite for sustainable development is to preserve the ability to meet the present and future human needs. In this regard, the development of new biomedical technologies and their introduction into clinical practice is a necessary process for the technological progress in controlling life expectancy. One of such technologies that can dramatically change the pharmaceutical field, is the use of nanodrugs. The latter represent the pharmaceutical formulation in which the drug is encapsulated inside the nanocarrier (nanoparticle). Application of nanodrugs can radically alter the pharmacokinetics and pharmacodynamics of the drug, due to its controlled release and controlled distribution in the body. This reduces the side effects of the drugs, enhances targeted delivery of drugs, and makes possible the delivery of the drug through complex biological membranes. All these factors could lead to an effective therapy of intractable and incurable diseases and can prolong personal life.

The treatment of skin diseases, as well as transdermal delivery of drugs, are of significant practical interest. The application of nanoparticles for this purpose is very promising. Different drugs administration strategies require different approaches for particles administration. For transdermal

drug delivery, which is perspective for overcoming the first path metabolism, the nanocarrier has to penetrate inside the skin via intercellular or transcellular pathways. The treatment of skin diseases could require the controlled release of drug from nanoparticulate formulation located somewhere in the follicle.

The research within the project was devoted to the development of systematic approach to elucidate the effect of nanoparticles (NPs) properties on their ability to penetrate skin layers. The polylactic acid (PLA) and polycaprolactone (PCL) based particles were obtained by two different methods: single emulsion and nanoprecipitation. The NPs sizes were estimated to be 340 and 82 nm, correspondingly. Such particles are quite hydrophobic and could be accumulated in subcutaneous layer. To modify the surface properties of the particles the methods of covalent attachment of charged natural polymers were developed. The surface of initial PLA and PCL NPs was estimated to be slightly negatively charged. In order to make the particles positively charged they were modified with poly-L-lysine (MW 30 kDa). Further electrostatic layering of heparine sulfate gave NPs with negatively charged surface.

In order to visualize the particles inside the skin, as well as to investigate the drug release properties the special fluorescent substance (pyrido[2,1-a]pyrrolo[3,2-c]isoquinoline) was synthesized at the Institute of Chemistry (SpBU, Organic Chemistry Department) and encapsulated inside the NPs.

The samples of obtained NPs were subjected to the investigation in the various research groups of FUB: Prof. Erckart Ruehl (Institute of Chemistry and Biochemistry, Raman spectroscopy and microscopy), Prof. Ulricke Alexiev (Institute of Physics, fluorescent properties of particles), Prof. Monika Schaefer-Korting (particles cytoxicity, NPs penetration into skin and drug release). The understanding of transdermal NPs penetration and fate, as well as release of model drug inside the skin, is within the scope of this still ongoing research.

The organizational part of the work in FUB was devoted to the understanding of research management principles. There are three main issues that could be distinguished in FUB and should be developed into SpBU: interdisciplinarity, cooperation, specialization.

First of all the research projects within FUB have comprehensive interdisciplinary character. It means that the problem is studied from different points of view and with various experimental approaches. For example, the project, which was aimed at creation of nanocarriers for transdermal drug delivery, involves physics, chemists, pharmacologists, biologists. Secondly, the cooperation between these groups is very strong and well-organized. The people involved into the project are opened to each other and easily participate into interdisciplinary research between different groups as well as in various meetings. Thirdly, it is important to note, that work distribution within the research group is based on the

specialization of each collaborator. It was very interesting to find out that there are special people within each research group, which are responsible for paper work. This allows the research staff to concentrate on the experimental work and preparation of publications. Professional managers and clerks seem to be very effective within the modern research team. From my point of view it is these key factors that makes FUB research quite successful and that should be taken into consideration by SpBU management staff.

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