Quaternary ammonium compounds (QAS)–*mono* are common in natural environment. They are produced by bacteria, fungi, invertebrates, vertebrates and plants. These are surface active substances, built of hydrophilic and hydrophobic part. The wide variety of QAS and their functions has been an inspiration for the scientists to synthesize new surfactants with various chemical structures and to use them in many fields of industry and medicine (e.g., as disinfectants, biocides, fungicides, as well as anesthetic drugs).**Common application of QAS as disinfectants is the cause of growing phenomenon of drug resistance among microorganisms. Thus, the invention of new surfactants with antimicrobial activity is very important. The potential candidates might be surfactants with complex structure (multifunctional or gemini).** Modifications of the chemical structure: number of hydrophilic and hydrophobic moieties, alkyl chain and spacer lengths or counterion type might enhance antimicrobial activity, biodegradability and decrease toxicity towards human cells. Our long standing studies allowed us to design new QAS with various chemical structures (architecture type, alkyl chain and spacer lengths, counterion type).

The purpose of the project is to investigate the relationship between the chemical structure of newly designed cationic surfactants (derivatives of hydroxybenzoic acid of different architecture type as well as gemini QAS with various alkyl chain lengths and different counterion) and their biological activity and ability to condense DNA. Literature data indicate that alkyl chain lengths, hydrophilic head structure and the type of spacer have major influence on the activity of surfactants. **However, there are no studies regarding the correlation between antimicrobial activity and the architecture type (linear, multifunctional and gemini).**

Due to the presence of hydrophilic and hydrophobic parts in the structure, cationic surfactants are able to interact with different surfaces. It is known that the longer hydrophobic elements, the stronger hydrophobic interactions will occur between surfactant molecule and the surface material. **This property allows quaternary ammonium salts to find potential application as surface coating agents**. **Deposition of cationic surfactants on silicone, plastic or stainless steel surfaces might efficiently block the microbial adhesion and prevent dangerous bacterial or fungal infections, as well as the development of resistant biofilms (difficult in eradication).**

The mechanism of action of cationic surfactants is not yet fully understood. It is believed that conventional, *mono*-QAS probably cause the disruption of plasma membrane and cell lysis, however at the lower concentrations they might interfere with lipid-protein interactions, inhibiting the activity of key enzymes. The mode of action of more complex surfactants may be dependent on their chemical structure. Gemini QAS may interfere with respiratory processes and increase plasma membrane permeability without causing cell lysis. On the other hand, multifunctional surfactants induce severe oxidative stress in yeast cells. **Thus, one of the project goals is to investigate the mechanism of action of proposed QAS on microbes with different cell envelope structure, and to determine whether there is a correlation between the architecture type of the surfactant and the mode of action.**

The essential feature of all amphiphilic compounds is the ability to form micelles in aqueous solution. Due to the presence of two hydrophilic and two hydrophobic compartments, **gemini surfactants may create more complex aggregates, like liposomal structures. Nowadays, liposomes are widely used as drug carriers and non-viral nucleic acid delivery systems in gene therapy, which are considered as more safe when compared to viral vectors.** The transfection of eukaryotic cells with lipoplexes (complexes of liposomes and nucleic acid) is a complicated process, influenced by many factors: efficient complexation of nucleic acid, transport through the plasma membrane via endocytosis, as well as the release of nucleic acid from the endosome and its import to the nucleus. The common issue is the toxicity of cationic liposomes towards transfected cells. **Thus, designed gemini QAS with various alkyl chain lengths are biodegradable, non-toxic and synthesized according to green chemistry rules.** Chemical structure of gemini surfactants (alkyl chain lengths, spacer and couterion type, hydrophilic moiety architecture) has a major impact on the efficiency of transfection. Long-chained compounds form liposomes at low concentrations and aliphatic spacer makes the molecule elastic and facilitates transition from lamellar to reverse hexagonal phase, what enables endosomal cargo release.

That is why surfactants with the highest capacity of complexing DNA will be selected among two series of gemini QAS (with various alkyl chain lengths and counterions, including chlorides, bromides, monomethyl carbonates, acetates, lactates) and tested for in vitro cell transfection.

The research described in this project will contribute to gaining knowledge about relations between **chemical structure of new quaternary ammonium cationic surfactants and their physicochemical properties, as well as their biological activity. These studies may also underlie the synthesis of new compounds with potential application as bactericides and fungicides, but also as efficient non-viral DNA carriers, that are able to deliver genes of any size to various types of cells.**