

The project proposal assumes development of a new biocompatible material with perspective application as local drug delivery system. The system will be soluble allowing its injection into desired part of body and it will undergo cross-linking directly in the desired place. The described system will contain molecules of cyclic oligosaccharide (cyclodextrin, CD) anchored to linear chain of polymer. Apparently CDs have form of truncated cone with internal cavity enable to receive other molecules forming host-guest complexes. In fact, it is known that the CDs form such host-guest complexes with various drugs improving solubility, stability and bioavailability of many drugs which are poorly soluble in aqueous media. In the project CDs possessing different sizes of the internal cavity as well as different affinity to water will be attached to the polymers and then possibility of incorporation of several types of drugs (antibiotics, anti-inflammatory drugs and cytostatics) into the polymer will be investigated. On the other hand, CDs form inclusion complexes with many other moieties among which is adamantane and its derivatives and these complexes are known to be very stable since adamantane fits in into CD cavity very well. One can picture polymeric chains bearing several CD complexes of drug each which will be mixed with linear polymers possessing adamantyl groups (many groups on each polymeric chain). In consequence adamantyl groups will get complexed with CD forming link between the two polymeric chains and in the same time releasing the molecule of drug which was carried in the CD cavity. Similar repetition of the process should result in formation of cross-linked structure where part of the complexed drug is replaced with adamantyl groups. The bursted drug acts in vicinity of the place the system is localized and rest of the drug is released slowly. If necessary, drug release can be accelerated by presence of adamantane (or its derivative) delivered with body fluids. It is also important that toxicity of adamantane is very low and it reveals interesting feature like passing through blood-brain barrier, so in fact if the delivery system is placed in brain cavity, it is possible to increase drug concentration in brain by simple introduction of adamantane while, because of blood-brain barrier existence, it is not that easy when drugs are administered classically. In fact, local drug delivery systems, releasing drugs in vicinity of the diseased tissue decrease amount of drugs which needs to administered to reach therapeutic level. It may be of interest to be aware that an intravenous injection of paclitaxel (highly toxic drug used in treatment of tumors) almost 50% is eliminated during the first 24 hours, with less than 0.5% of the total dose locally available to treat tumor within the lung. Moreover, local drug delivery systems are used for treatment of rheumatological conditions, and delivery of antibiotics, especially after implantation of orthopedic devices. However, to develop such a system it is crucial to understand how much of particular drug can be delivered in which type of CD (actually if any) and how much drug will be released after the system is located in its destination. It is also important to confirm that the bare system will not cause any undesired effects when placed in living organism and to understand how long the system can work.

Driving force to undertake this research is increasing number of cases and broad range of diseases where local drug delivery is more effective then methods used for decades. In junction with clinical results showing superior effect of local drug delivery over classical methods development of such systems seems to be needed urgently.