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APPLICATION OF NANOFIBERS AS DRUG DELIVERY SYSTEMS

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Summary: This paper describes the results of our preliminary studies on Drug Delivery Systems. Two distinct types of drugs are being investigated: lipophilic (soluble in organic solvents) and hydrophilic (soluble in water). Direct measurements of drugs and dye release from nanofibers were done for application in an animal model-rat.

The electrospinning (electrostatic spinning) is comparatively cheap and versatile method of production of micro- and nanofibers. Such nanofibers are of potential use as scaffolds cell cultures and for tissue engineering. The Electrospinning Group of Department of Mechanics and Physics of Fluids IPPT PAN investigates both the fundamentals of the electrospinning process as well as the medical applications of the electrospun nanofibers as the protective material and drug delivery systems for neurosurgery. The production of nanofiber-based Drug Delivery Systems (DDS) has currently driven our attention. Two distinctive systems are necessary to deliver different types of drugs on basis of their properties. Lipophilic drugs (soluble in organic solvents) can be easily dissolved in the solution of polymers for electrospinning. If no phase separation occurs in nanofibers produced and the drug is well soluble in a polymer matrix it is possible to produce DDS of well-defined release pattern (Fig. 1 and Fig. 2).

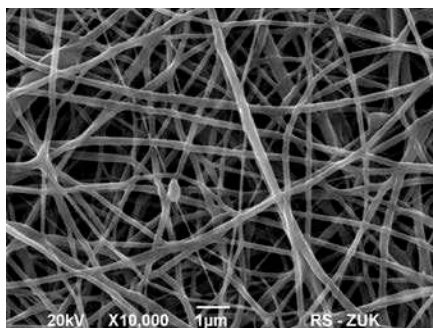


Fig. 1. SEM micrograph of a nanofibrous mat containing 15% of alpha-tocopherol.

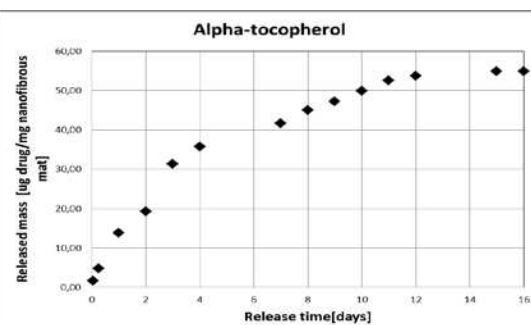


Fig.2. Release of alpha-tocopherol from nanofibrous mat. The drug was released for at least 2 weeks

Fig. 1 shows the appearance of electrospun membrane made of nanofibers. The mat does not contain defects. Fig. 2 shows the release of a model neuroprotective drug – alpha-tocopherol. No burst release of the drug was noticed. The release time as well as the amount of released drug (ca. 0.55% per mass of DDS) makes this system a good candidate for a pilot study for animal model of traumatic brain injury.

It is far more complicated to produce DDS for drugs insoluble in the organic solvents (hydrophilic). Such drug cannot be incorporated directly in a polymer matrix structure. In emulsion electrospinning solution of the drug in water is emulsified in the electrospinning solution to produce micro-nanofibers that contain drug reservoirs. We produced DDS releasing sodium glutamate (potential neurotoxic agent). Since the direct measurement of drug concentration is laborious we developed a method for indirect measurement of water-phase release of a dye – Methylene Blue.

Figs. 3 and 4 show a release of a drug and dye from emulsion electrospun mats. The release profile for dye (Methylene Blue) was qualitatively similar for drug and dye released from electrospun DDS. The dye release can be used for assessment of drug release for projected DDS releasing water soluble drugs.

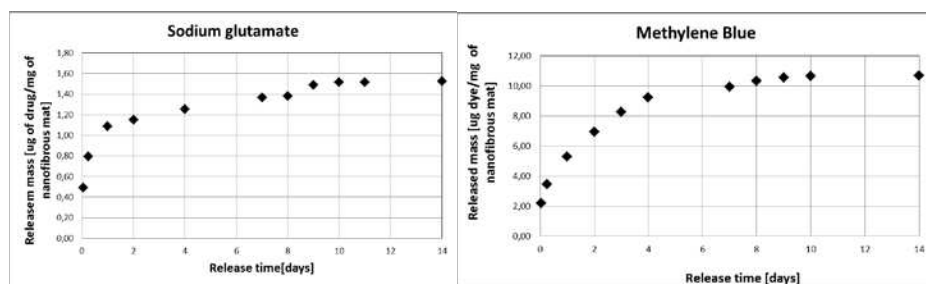


Fig. 3. Release of sodium glutamate from emulsion electrospinning. Drug concentration: 0.62 % of mass of nanofibrous mat.

Fig. 1. Release of Methylene Blue from emulsion electrospun mat.

Conclusions. Two Drug Delivery Systems produced by electrospinning of nanofibers have been successfully prepared for the use on pilot studies on animal model of brain injury or neurodegenerative disease. Both amount of the drug loaded onto a DDS and the amount of drug released is higher for a lipophilic drug than for hydrophilic. Single phase electrospun DDS offer higher drug release than the emulsion DDS.

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