SHORT TERM SCIENTIFIC MISSION (STSM)
SCIENTIFIC REPORT

This report is submitted for approval by the STSM applicant to the STSM coordinator

Action number: CA17107
STSM title:Fabrication of novel biodegradable composite fibers for drug delivery systems
STSM start and end date: 13/09/2021 to 30/09/202
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PURPOSE OF THE STSM:

The main purpose of the short-term scientific mission was the production of composite smart textile, consisting of polymer fibers with cellulose-based hydrogels, suitable for use as drug delivery system (DDS). Biodegradable polymer fibers belong to a new class of polymer materials and what sets it apart from the other commonly used polymers is that it can carry hydrophobic (into the polymer fibres) and hydrophilic (into the polymer gels) drugs. Wet spinning and also novel technique-electrospinning methods were ideal techniques for this. Electrospinning is a well-known method for fabrication materials for medical use. In this way, it is possible to obtain a polyurethane composite material suitable to use as carrier of the drug substance. The composite fibers used was polylactide and alginate which are biodegradable and biocompatible polymer.The purpose of the short-term scientific mission was to strengthen communication, establish new relations and exchange results between institutions and with people who are working in the field of my novel research interest which could lead to possible fruitful collaborations.

DESCRIPTION OF WORK CARRIED OUT DURING THE STSMS

During STSM, four types of carboxymethylcellulose (CMC) hydrogels were synthesized. CMC hydrogels were synthesized with two different types of crosslinkers (citric and adipic acid) at two crosslinker concentrations of 1% and 2 wt%. After synthesis, the hydrogel samples were tested by FTIR and DSC method and the degree of swelling of the samples was determined. The samples were ground and sieved through a 0.9 mm sieve. In the second week, a composite smart textile was prepared from alginate and hydrogel. The active ingredient, amoxicillin, is incorporated into the hydrogel. First, the hydrogels are swollen in the drug dispersion in water, but only at 100% swelling (about 2 minutes). Since these hydrogels have a swelling rate of about 400%, in order to ensure that the hydrogel absorbs the entire amount of the drug, it is necessary not to bring it to the maximum degree of swelling. The gel was then dried for about 24 hours at room temperature and then transferred to a polymer solution, alginate in water (5% solution). It was decided for this polymer matrix regarding hydrogel and medicinal substances, because alginate is the most commonly used polymer for biomedical use, and it is non-toxic and easily degradable, its solvent is water, which is also non-toxic. The only problem is hydrogel swelling in water, so the process of extracting the fibers had to take place very quickly. The amount of hydrogel added to the polymer solution was 10% by weight of the polymer, while the amount of antibiotic was 10% by weight of the hydrogel. After mixing the hydrogel into the polymer matrix, the fibers were extracted using two methods: by drawing from a syringe into a solvent-acetone and by electrospinning. Electrospinning had a very pronounced problem with the swelling of the hydrogel, so the passage through the needle was very difficult, due to the long retention of the solution in the syringe, so the process went nicely, the fibers were uniform during the first hour, after which the solution was difficult to pass through. syringe and there was

an agglomeration of hydrogels in the structure of the electrospinned fiber. In this way, the gel is not coated with a membrane made of polymer fibers, but is immersed in the fiber itself. The gel was outside and could easily release the medicine. After obtaining the nanocomposite fibers, they are glued to a polymeric carrier - in our case polylactide film, thus obtaining a material that can be used as a patch. Samples of pure hydrogels on the polylactide film and samples with amoxicillin inside the hydrogel were made. The resulting nanocomposite fibers were examined by HPLC, monitoring the amount of drug released over time. The antimicrobial activity of the obtained polylactide/hydrogel patch was also examined. The test was performed on bacteria: *Escherichia coli, Staphylococcus aureus, Bacillus cereus, Listeria monocytogenes, Pseudomonas aureginosa, Salmonella Typhymurium, Enterococcus feacalis*. These bacteria were chosen because the human body most often encounters them, and amoxicillin is one of the drugs used for these bacteria.

DESCRIPTION OF THE MAIN RESULTS OBTAINED

The obtained results of hydrogel testing on FTIR showed that there were no residual monomers in the samples. There was no significant difference between the samples with different crosslinkers and different amount of crosslinkers. DSC results show good thermal stability of all hydrogels, at the temperature of application, which is very important for materials used in biomedicine. Examination of the degree of swelling showed that carboxymethyl cellulose hydrogels have a degree of swelling of 300-450%, with the fact that the hydrogels decompose at the maximum degree of swelling, this is an important fact in order to avoid the state of hydrogel decomposition during application. Here it was shown that samples with adipic acid as a crosslinker give a lower degree of swelling, 300-350%, while samples with citric acid give samples with a degree of swelling 400-450%. When preparing alginate samples with hydrogels, the swelling property proved to be a very important item, because during the preparation it was shown that the hydrogel with a lower degree of swelling is more suitable for the microfiber extraction process. Two methods for the preparation of alginate microfibers with hydrogel and amoxicillin in the microfiber structure (syringe extraction method and the electrospinning method) were used. By drawing the fibers from the syringe into acetone, all the fibers were of uniform structure, but this process proceeded rapidly, about 20 min per sample. While a structure that was not uniform in places was obtained during electrospinning, probably due to the long retention of the hydrogel in the alginate solution with water, so that the hydrogel swelled (2 h) during the process was heavier, and therefore the fibers less uniform. During the electrospinning process, the hydrogel with 2% crosslinker, adipic acid, proved to be the best, because the samples were the most uniform, while the process lasted until the very end without any problems of passing through the electrospinning needle. After drying the microfibers at room temperature, the fibers were glued to a polylactide film carrier to obtain a patch for targeted use on the skin. The samples were tested by HPLC method, for 24 h, because amoxicillin was used for 24 h. The results of the HPLC method showed that drug release was the fastest in the first 4 h by releasing a large amount of drug and then releasing gradually decreased. Antimicrobial analysis confirmed that the patch samples had antimicrobial activity because a circle appeared around the samples (during antimicrobial testing), which is evidence that the material is antimicrobial. These results are a good basis for further research work. Successful production of porous fibrous nets with built-in cellulose-based hydrogels provides an opportunity for their further upgrading as a drug for application in the body and on the skin as a wound dressing.

FUTURE COLLABORATIONS (if applicable)

After three weeks of STSM and preparation and testing samples at Faculty of Technology, University of Novi Sad further joint work on the same samples is planned. The contribution from the application and characterization of the samples has greatly contributed to the new ideas for the testing of hydrogels and composite of electrospinned polymer and hydrogels and the possibilities of their application. Additional collaboration is planned on the characterization of samples already made and co-authored works planned over the coming months, the plan is to expand collaboration and continue on current samples and projects, and then extend the collaboration to other areas of work. It is hoped that this will establish good cooperation and the backbone for writing some joint projects in the near future.