Diabetes mellitus is a chronic metabolic disease of civilization in which the pancreas does not produce a sufficient amount of insulin, a hormone that regulates blood glucose level. Hyperglycaemia caused by diabetes results in damage to many body systems, especially nerves and blood vessels. A serious complication of diabetes are hard-to-heal ulcers of the foot, the so-called diabetic foot, which can lead to limb amputations. The number of amputations that are complications of diabetes is increasing every year due to the lack of effective treatments.Generally, diabetic foot ulcers treatment, beside the regulation of blood glucose level, is based mainly on topical therapy. In the field of topical therapy, hydrogel dressing are of particular interest, providing the ulcerated area with adequate hydration, as well as protection from infection caused by bacteria. Nevertheless, hydrogel dressings have a number of limitations that reduce the effectiveness of diabetic foot treatment, such as poor mechanical properties or too rapid degradation of the dressing. It is now established that both infections and high concentrations of reactive oxygen species, which can be regulated by fat-soluble vitamins A and E, are major causes of limb amputations. In addition, the high susceptibility of diabetics to fungal infections requires the inclusion of antifungal drugs in topical treatment. However, these drugs are difficult to dissolve in water making their encapsulation in hydrogel dressings difficult. In addition, the use of other hydrophobic therapeutic substances with beneficial effects on diabetic foot ulcers, such as vegetable oils for example olive oil, is also limited with hydrogels. For these reasons, hydrogel dressings developed to date are not optimal and are still not widely available. Efficient treatment of the diabetic foot using dressings can only be achieved if adequate hydration and antimicrobial protection of the wound is provided with simultaneous delivery of both water- and fat-soluble drugs. Therefore, it is necessary to develop a new type of dressing materials, providing encapsulation of both water-soluble and fat-soluble drugs and with sufficient durability to ensure the effectiveness of treatment

T**he aim of this project is to synthesize bigel materials for the treatment of diabetic foot ulcer adapted to different stages of the disease, i.e., from shallow to deep wounds with observed vascular atrophy.** Such materials, thanks to combination of hydrogel and oleogel domains, will provide the wound moistening and sustained simultaneous delivery of hydrophilic and hydrophobic bioactive substances. With the proper selection of the method and the degree of cross-linking of the two phases, we can obtain injectable biphasic dressing materials that adapt to the tissue defect. This ensures direct contact with the tissue, wound protection and effective delivery of therapeutic substances.
In this project, we will exploit a new method of making bigels based on controlled crosslinking of oil-in-water emulsions using biocompatible hydrophilic and hydrophobic copolyethers to produce well-defined biphasic gels suitable for treating diabetic foot ulcers at different stages of disease progression. We plan to use two mechanisms to crosslink macromolecules, such as the Diels-Alder cycloaddition reaction and the formation of boronic esters, which are neutral to all encapsulated bioactive substances. Using these mechanisms, we avoid the unfavourable, both for ulcer healing and the structure of the applied bioactive substances, effects of radicals commonly used in the crosslinking of hydrogels.
The conducted research will provide the necessary knowledge about the influence of the structure of the individual building blocks of the two-phase polymer network on the properties of the bigel in the perspective of its use as a matrix for controlled delivery of hydrophilic and hydrophobic drugs. The knowledge gained will help answer the question of how we can control the mechanical properties of bigels, their permeability to compounds of various solubility, while maintaining its biocompatibility. The results of the conducted research will allow to design bigels with the appropriate composition and properties, optimal for the treatment of diabetic foot ulcers at different stages of the disease development. In addition, the results obtained will also be valuable in the perspective of designing other dressing materials dedicated to the treatment of hard-to-heal wounds, such as, for example, burn wounds.