**1. Purpose of the conducted research/research hypothesis**

Treatment for chronic wounds is one of the most complex therapeutic problems of modern medicine, as well as economic challenges because the prolonged recovery of patients generates high costs for their treatment. Scientists constantly looking for new compounds with multidirectional effects on the chronic wound healing process, simultaneously stimulating immune processes, inhibiting bacterial infections, influencing growth factors, and accelerating skin regeneration as well as more effective methods of active compound administration. Plant raw materials and their active compounds have many valuable biological activities, including antimicrobial, antioxidant, anti-inflammation, angiogenesis-stimulating, keratinocyte and fibroblast proliferation and migration-stimulating, growth factor-activating properties, which can significantly influence chronic wound healing mechanisms and find their application as active ingredients in wound dressings. To take full advantage of the multidirectional effects of plant raw materials and the wide range of their biological activities that can beneficially influence the healing processes of chronic wounds, mixtures of different plants and active ingredients of plant origin should be created.

The research hypothesis: *The addition of plant-derived compounds to Rhodiola rosea extract enhances its wound healing activity in in vitro study on cell cultures and in in vivo study in diabetic pig model.*

**2. Research description**

*Experiment 1. Determination of the biological activities of mixtures of R. rosea extract and plant-derived compounds as potential raw materials with a multidirectional stimulating effect on the wound healing process – in vitro study.*

The biological activity of plant mixtures will be determined by performing assays for (1) cytotoxicity, (2) antimicrobial activity, (3) antioxidant activity, (4) skin cells proliferation and migration capacity, (5) anti-inflammatory effects, (6) effect on growth factors in skin cells, (7) angiogenic activity, (7) effect on collagen and hydroxyproline synthesis in fibroblast. Selected mixtures of plant-derived compounds and *R. rosea* extract with a multidirectional mechanism of action, significantly stimulating biochemical processes related to the phases of diabetic wound healing will be used as active ingredients in the preparation of wound dressings.

*Experiment 2. Development of wound dressings containing selected mixtures of plant-derived compounds and R. rosea extract with optimal release profile of active ingredients.*

The wound dressings will be made according to the principles of bioactive dressings that promote wound healing and are made of substances naturally occurring in the human body, without causing allergic or immune reactions. The gel part of the dressing will be made from polyesters based on biomimetic raw materials. The performance characteristics of the dressings will be determined by characterizing: (1) mechanical properties of the dressing after soaking, (2) porosity and water absorption, (3) tensile strength, (4) absorption capacity of the active compound into the patch, (5) release profile of the active ingredients from the dressings, (6) antibacterial activity of the dressings. Selected plant mixtures-loaded dressings with favorable release profiles from the dressing will be used in experiment 3.

*Experiment 3. Determination of the effect of a mixture of plant-derived compounds and R. rosea extract on the wound-healing process in STZ-induced diabetic pig model - in vivo study.*

The experiment will be performed on pigs, randomly divided into groups without diabetes and a group with type 2 diabetes induced by intravenous administration of streptozotocin (STZ). On the dorsal side of the pig with full-thickness skin excision will be placed dressings (with plant mixture/control without dressing (gauze) / positive control - povidonum iodinatum) in both animal groups. Dressings will be changed every three days for the duration of the experiment (21 days). Determination of wound healing activity of plant mixtures-loaded dressings will be included: (1) evaluation of wound closure, (2) evaluation of wound contraction, (3) histological analysis, (4) immunohistochemical analysis, (5) determination of inflammatory mediators, (6) determination of growth factors, (7) determination of antibacterial activity of plant-loaded dressings against bacteria isolated from wound fluid.

**3. The most important expected research results**

Understanding the biological mechanism of action via the mixture of *R. rosea* extract and the plant-derived compounds may influence different phases of the wound healing process, especially in diabetic individuals, and may be valuable for both pharmacy and medicine and in the future, form the basis for further clinical trials. Obtained results could be also valuable for veterinary medicine because the problem of healing wounds is one of the most common reasons for medical consultations in the case of diabetic pet animals.