Final Report

Project acronym: PELARGODONT

Project number: 4048

M-ERA.NET Call 2016

Period covered: 02__/05_/2017_ to 30/_07_/2019_

Refer to beneficiaries when filling out this report.
To be completed by the project coordinator only.
Minimum font size is 11 pt.

2. Publishable project summary

Focus on methodology, results and conclusions (max. 1 page).
Please note: The publishable summary will be used for dissemination by M-ERA.NET and the EC.

The aim of the project is to engineer a biodegradable drug delivery system of local action with natural active substance - *Pelargonium sidoides* DC. root extract (PSRE) or proanthocyanidins (PACN), isolated from this extract, for periodontitis treatment. Four innovative products have been created – collagen hydrogels (with 20% PSRE or 20% PACN) and gellan gum hydrogels (with 30% PSRE or 20% PACN). Microbiological tests of the active substances showed that PSRE and PACN exhibited antimicrobial activity against oral bacteria - Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, Streptococcus salivarius. PSRE aqueous solutions have reduced the viability of pathogens that cause periodontitis: P. gingivalis, A. actinomycetemcomitans, and the symbiont - S. salivarius. The PCAN aqueous solutions (0.05-0.09 mg / mL) reduced the viability of P. gingivalis and A. actinomycetemcomitans ($p < 0.01$) compared to control, while the viability of the symbionts S. salivarius bacteria remained unchanged. By developing a medical anti-bacterial device for long-term use, it is important to suppress the vitality of the pathogenic microflora alone, while also being safe, i.e., protecting bacterial symbionts in the oral cavity. In vitro study of the effect of the developed composites with active substances on cell cultures was performed. All of the polymeric composites developed with PACN reduced keratinocytes proliferation and viability but activated hBMSC cell proliferation and viability. Polymeric collagen and gellan gum composites with PSRE activated cell proliferation of both keratinocytes and hBMSCs. Collagen hydrogels did not exhibit the required adhesive properties, whereas gellan gum hydrogels exhibit a higher swelling capacity to provide the necessary adhesive properties. The developed prototypes were tested in a randomized clinical trial of 97 patients with chronic periodontitis and 40 healthy
(control) subjects. All patients with chronic periodontitis were treated according to the standard conservative protocol for the treatment of chronic periodontitis (oral hygiene and root smoothing and curettage) with different adjunctive therapies: 1. placebo (E0); 2. E1 patient group - collagen hydrogels with active substance PACN were introduced into the periodontal pockets; 3. E2 patient group - collagen hydrogels with active substance PSRE were introduced into the periodontal pockets; 4. E3 patient group – gellan gum hydrogels PEL68 with active substance PSRE were introduced into the periodontal pockets; 5. E4 patient group – gellan gum hydrogels PEL69 with active ingredient PACN were introduced into the periodontal pockets. The results of the study showed that the influence of hydrogels treatment on reducing probe periodontal pocket depth, probing bleeding, and plaque index in all groups of patients receiving these adjunctive therapies was statistically significant. The reduction in probed periodontal pocket depth was statistically significantly greater in patients receiving hydrogel-saturated PACN or PSRE as compared to placebo. For the treatment of periodontitis with adjuvant hydrogel therapy with PACN or PSRE, concentrations of MMP - 3 were reduced in saliva specimens of all groups of patients using gellan gum hydrogels therapy with PSRE. The concentration of TIMP - 1 in the saliva samples of patients in this group increased. TIMP-1 reduces the activity of one of the most active inflammatory metalloproteinases, MMP-3. In all patient groups there was a statistically significant reduction in TAS (total antioxidant expression) in saliva samples when comparing pre- and post-treatment (both manufacturers hydrogels with PSRE and PACN). The physical properties of collagen hydrogels with PACN and PSRE at 5 ± 3 ° C remained unchanged during 12 months. The concentration of active substance in collagen hydrogels with PACN was statistically significantly less than that in collagen hydrogels with PSRE. The preferred sterilization method for collagen hydrogels was UV and gamma radiation, which did not affect the stability of the hydrogels. Gelan hydrogels with PACN and PSRE lost the stability of physical parameters after 3 months.