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POLYNUCLEOTIDES IN DENTISTRY

Abstract. *Topicality of the chosen theme is stipulated by research and introduction of polynucleotides as reparatives at therapy of periodontal diseases.*
Keywords: *polynucleotides, repair, regeneration, periodontitis, fibroblasts.*

Topicality of the topic. Treatment of periodontal diseases is one of the most important and complicated problems of stomatology, the urgency of which is conditioned by high frequency of inflammatory periodontal diseases, appearance of foci of chronic infection, premature tooth loss, decrease of psychoemotional status, work capacity. Progressive loss of the basic functions of the periodontium and the dentoalveolar system as a whole is promoted by the decrease in the body's resistance to the action of external negative factors, its sensitization and intoxication [1]. Among periodontal diseases, gingivitis is the most common form of parodontal tissue damage and occurs primarily in children, adolescents, and persons under 35 years of age, as it further progresses to periodontitis if not treated [2,3]. For the time being, local injectable drug therapy using hyaluronic acid-based products has gained momentum in the treatment of periodontal disease.

However, not so long ago one of the innovative promising discoveries, a new word appeared - polynucleotides. Polynucleotides (polydesoxyribonucleotide or PDRN) are biopolymers, natural fractions of DNA, they can activate physiological cellular regeneration through direct stimulation of fibroblasts. The result is increased

fibroblast regeneration and increased production of collagen and extracellular matrix proteins, including hyaluronic acid. [4]

By their structure, polynucleotides or PDRNs are elements of low molecular weight DNA, which do not cause genetic transformation and are safe for humans. They are a building biomaterial that restores the intercellular space of our body from within. Having an immunomodulatory effect, they stimulate regeneration and repair processes, enhance the synthesis of elastin, collagen and non-collagen molecules, and have anti-ischemic and anti-inflammatory properties [5]. For modern preparations, polynucleotides are derived from organic raw materials. They are a special extract from the DNA of the gonad tissue of male salmonids. Since the DNA of salmonid fish milk and human leukocyte DNA are very close, that is why the PDRNs work perfectly in the human body. [6] Milk is rich in nucleic acids and protamine proteins, which have been successfully used in medicine for 100 years. Preparations based on polynucleotides extracted from salmon's milk do not cause allergic reactions or other serious side effects, so they are safe for humans, but as for any therapeutic drug in this world, it is still worth doing a test run.

Introduction:

At the moment, the importance of effective treatment of periodontal and oral mucosa diseases has increased many times, according to numerous studies, polynucleotides are a new and advanced method of treatment in our time.

In my work I studied an actual, effective and safe way to treat gingivitis and paradontitis with preparations of polynucleotides, the use of which will make a huge step forward in dentistry.

Mechanism of action:

- stimulate tissue repair and regeneration;

- Increase the metabolic processes in the cells;

- Increase production of collagen, elastin and non-collagen molecules by fibroblasts;

- accelerate scarring and reepithelization;

The mechanisms of action of polydesoxyribonucleotide drugs (PDRN) are their influence on endogenous colony-stimulating factors, production and differentiation of hematopoietic progenitor cells, but the most important is their immunomodulatory effect, especially - with regard to the impact on regeneration and repair processes[7] In particular, stimulating the functional activity of monocytes/macrophages PDRN increase their ability not only (and not so much) phagocyte microbes and damaged tissue structures (including damaged collagen and elastin), but also the function of antigen presentation, thus significantly influencing both T- and B-links of the immune system, and through them - the entire complex of the unified neuroimmunoendocrine regulatory system (ENIERS). [8]

We should also note the possibility of other influences on the organism of DAW drugs. For example, when patenting an injectable composition of PDRN for the treatment of bone and joint diseases, Cattarini Mastelli Laura and Cattarini Mastelli Giulia noted that PDRN macromolecules are exposed to the action of lytic enzymes, which gradually release smaller and smaller polynucleotides and their structural components into the joint cavity, which is used by tissues to improve cell activity and protection as well as to activate physiological regenerative mechanisms.[9]

More than 30 years ago, tests were conducted to develop effective treatments for diseases related to ionizing radiation. Among the biologically active substances tested was deoxyribonucleic acid (DNA) extracted from the gonadal tissue of male salmonids. The extract was carefully purified, depolymerized, and balanced with sodium hydroxide according to a documented procedure.[17,18]

The extract was later named polydisoxyribonucleotide (PDBN) according to the International Nomenclature of Cosmetic Ingredients. Positive feedback on polydisoxyribonucleotides was received in 1986, when they were used to treat illnesses related to the Chernobyl accident. PDRNs act as stimulants to restore cellular activity.

MDPN passes through cell membranes by pinocytosis (Fig. 1); the endocytosis method is provided by sodium ions that bind to polydesoxyribonucleotides. As a

consequence, cells presumably use the resulting amount of PDRN as a structural basis for the synthesis of nucleic acids and their co-acting factors, as well as for the transformation of their own DNA. These processes occur very readily in cells that are in a state of reduced metabolism or under stress. Functional activity of "aged" keratinocytes and fibroblasts is restored. Thanks to the cellular integration process, the PDRNs work as a stimulant to enhance regeneration and reduce the symptoms of inflammation, thus improving the healing of microdamages in the skin.

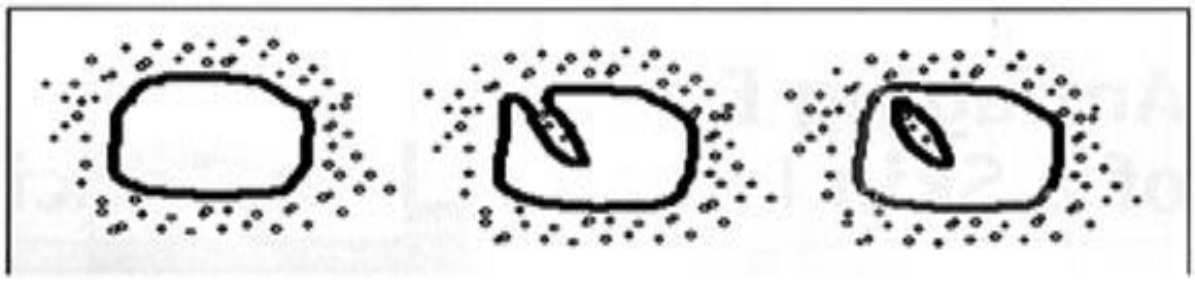

Fig. 1 Pinocytosis as a method of transferring exogenous molecules into cells

Additional studies and evidence-based materials on the use of PDBN in the process of activation of tissue regeneration and repair in pathological processes of different genesis. The use of polydeoxyribonucleotides (PDBN) proved to be effective for tissue repair in peripheral arterial occlusive disease, diabetic foot ulcers. The efficacy of PDRN in wound healing has been proven using a cellular substrate electrical resistance (CSEC) measurement system and a viability test. [10]. Human osteoblasts (U2OS-cells) and primary human dermal fibroblasts (HDF-cells) were used to study the effect of HRPN on migration and proliferation. Using the IESC system, a wound was formed by applying a high voltage current and then the wound healing process was monitored by measuring resistance in real time. Cell migration by culture insertion and gap closure was analyzed and compared with the IESC wound healing assay. U2OS and HDF cells, to which PDRNs were applied, affect cell migration to the site of injury. The viability test showed that the proliferation of HDF and U2OS cells was dependent on the concentration of PDPRN. (Figure 2). Thus, PDRNs demonstrated their effectiveness in healing bone and skin lesions.

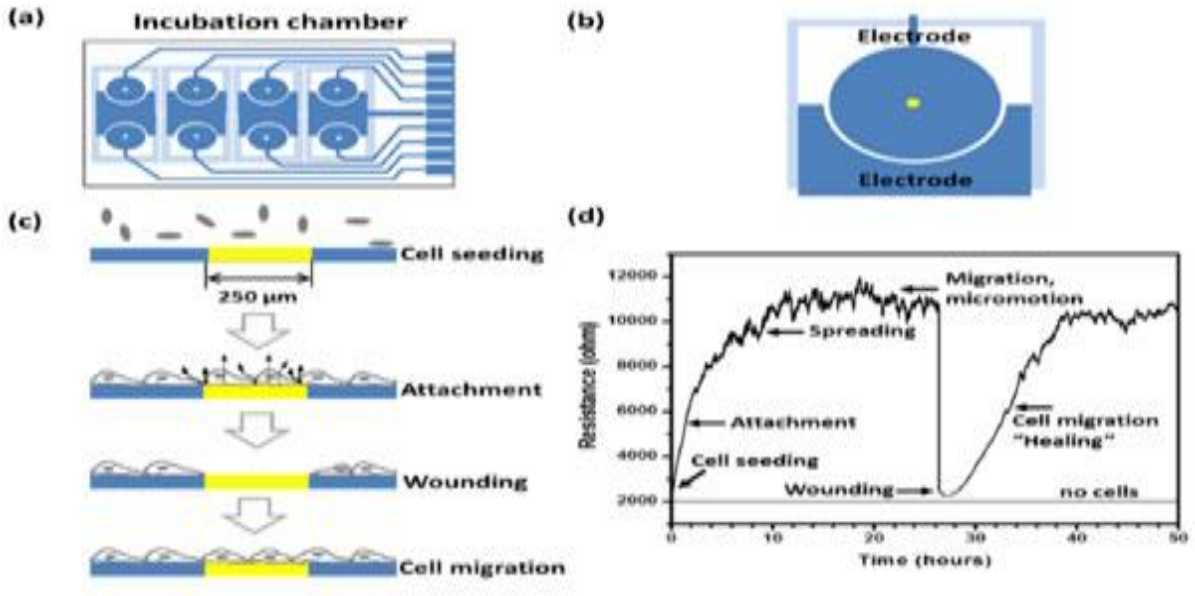

Fig. 2.

We studied the effect of PDRN on diabetes-related treatment disorders using a model of an incisional skin wound defect on the back of female diabetic mice and their normal littermates (Department of Clinical and Experimental Medicine and Pharmacology, Department of Pharmacology, University of Messina, Messina, Italy). [14]. During the experiment, the scientists found that the use of PDBN improved wound healing in diabetic animals compared to placebo. PDPRN markedly increased the activation of FRES (vascular endothelial growth factor) as well as mature protein in the wounds. This indicates that in diabetic mice, FRES mRNA levels as well as FRES content in wounds were severely reduced under normal conditions, thereby impairing the healing process.

In addition to FRES, PDRN increased the expression of angiopoietin-1, an angiogenic factor involved in the stabilization and maturation of newly formed vessels. Since the physiological and efficient development of blood vessels occurs through the synergy and interaction of these two factors, it is reasonable to assume that the study obtained near-normal blood vessel development. In addition, these data suggest that the effect of PDRN is not selective for FRES, but can affect several factors involved in the healing process. In addition, the effect of PDRN on FRES can result in a controlled inflammatory process. The interaction occurs through specific receptors (A1, A2A,

A2B, and A3), especially expressed in all cellular components of wound healing, including neutrophils, macrophages, fibroblasts, and endothelial cells. [11]

Under the influence of certain enzymes, PDRN decompose into active components, in particular adenosine, which leads to interaction with adenosine receptors (A1, A2a, A2b) of immune system cells. Due to this the production of inflammatory mediators decreases, the action of pro-inflammatory IL - 12, tumor growth factor (TNF - a) is inhibited. Production of IL - 10, a powerful anti-inflammatory cytokine, is activated. Thereby the proliferation of endothelial cells is regulated and angiogenesis is induced by restoring the synthesis of vascular endothelial growth factor (VEFG). Parallel restoration of fibroblast activity and matrix derivatives in the complex enhance and activate regeneration and repair processes in case of tissue damage.[11,12,13]

It has also been determined that the molecular effects of PDRN are carried out on both epidermal regeneration and granulation tissue thickness, fibroblast formation, and the emergence of new, well-structured, capillary vessels. The latter also confirms that the development of blood vessels, along with cell migration, inflammation, temporary matrix synthesis, collagen deposition, and reepithelialization, is crucial in the process of skin repair. Moreover, trichrome Masson staining showed a stimulating effect of PDRN on fibroblasts with the formation of augmented granulation tissue. This finding is supported by increased expression of tissue transglutaminase, a molecule called the "natural" glue in the intercellular matrix, which plays a key role in all the repair processes that occur during healing

Dental applications:

In dentistry, this innovative product PDRN can be injected together with HA (hyaluronic acid), as the former enhances and prolongs the action of the latter. It has an anti-inflammatory effect, inhibits the reproduction of pathogenic microorganisms in the inflammation focus, powerfully stimulates metabolic processes in cells, restoration and their division, accelerates the regeneration of damaged tissues, so it can be used as a treatment for periodontal disease.

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