Evaluation of the Role of the Body's Response to Skin Damage in Experimental Diabetes Mellitus Based on Individual Typological Reactions of the Body

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ABSTRACT

In modern experimental diabetology, chemical models of diabetes occupy the first place, and various methods of QD experimental model are used in the field of enteropharmacology. Alloxan diabetes occurs as a result of the use of alloxan in animals, which develops necrotic processes in the pancreas, and then the symptoms of diabetes appear. Modeling of skin defect in animals with different individual typological reactions in experimental diabetes and comparative analysis of skin tissue regeneration in 60 rats. It is planned to divide animals by typological category (groups): "sympathetic-active" and "parasympathetic-active".

Keywords: Alloxan diabetes, low emotionality, high emotionality

According to WHO, 8.5% of the population aged 18 years and older suffer from diabetes mellitus (DM) (2014), among which the death rate is 1.6 million (2016), and the death rate due to high blood sugar is 2.2 reaches a million (2012). According to the projections of the World Health Organization, the number of people with diabetes mellitus (DM) will reach 552 million by 2030 [Whiting D.R. et al., 2011]. Of these indicators, the percentage of patients with type 1 QD is about 10% [Stanekzai J. et al., 2012]. The main reason for the development of type 1 diabetes is the destruction of the beta cells of the pancreas, which produce and secrete insulin, and the decrease in the production or insufficient secretion of insulin by these cells. The seriousness of the problem of diabetes is that it causes the development of severe complications, such as the ulcerative necrotic process of the skin, which leads to more severe complications in the form of diabetic heel syndrome (DTS).Such changes are partly the result of the pathological condition of the peripheral nervous system, arterial and microvessels, and then deep disability and a significant decrease in the quality of life. In patients with a long-term (more than 10 years) disease, dystrophic changes in the skin increase to 75-85% with the further development of ulcers. According to world statistics, purulent-necrotic skin complications account for 46% of all patients hospitalized with diabetes mellitus (DM) within 1 year. In modern experimental diabetology, chemical models of diabetes occupy the first place, and according to the literature, various methods of experimental model of diabetes were used in the field of enteropharmacology from 1996 to 2006. Thus, streptozotocin was used in 69% of cases and alloxan in 31% of cases [7, 15]. Among the chemical models, streptozotocin and alloxan are the most common drugs used to induce experimental diabetes. Streptozotocin (streptozocin, isostocin, zanozar) is a synthetic drug obtained from Streptomyces achromogenes microorganisms, hence the name. Alloxan diabetes is caused by the administration of alloxan to animals, which

develops necrotic processes in the pancreas and develops the first symptoms of diabetes [Malaisse W.J. [et al.] Pancreatic uptake of alloxan // Int J. Mol Med. [2-(14) C] 2001. V. 7. P. 311-315]. Pharmacological repair of skin wounds in diabetes is still the most complex process in regenerative medicine, but the use of fibroin obtained from Bombyx mori silkworm silk in the form of bandages and ointments is a very new trend in modern biomedicine. Fibroin is a native, biocompatible, non-toxic natural polymer, and the degradation of fibroin in the body is accompanied and controlled by the formation of non-toxic and, in some cases, even useful products for regeneration. As you can see, the chosen direction can be used in modern medicine in a timely manner.

The purpose of the study: to study the role of the body's reaction to skin damage with pharmacological correction, depending on the individual typological reactions of the body in the conditions of experimental diabetes

Material and research method.

Rats in the experiment were divided into 2 groups.

1 - bandage (gauze) in animals with low sensitivity.

2 - bandage (gauze) in animals with high sensitivity.

Diabetes was induced by alloxan in rats under experimental conditions. A wound was made on the skin, and it was decapitated in order to check the morphological changes that occurred after the traditional treatment. The isolated skin tissue was studied histologically using the hematoxylin-eosin method. Tissue pieces fixed in 10% neutralized formalin for 72 hours were washed in running water for 3-4 hours, then dehydrated in 70, 80, 90, 96, 100% alcohols and chloroform, and blocks were prepared by embedding in paraffin wax. The paraffin in the sections was removed by melting with xylene in a 57oC thermostat, and then stained in hematoxylin-eosin solutions to study the general histological condition of the tissues. The following changes were detected in the obtained micropreparations. When diabetes was initially induced in rats, vascular reactions were observed microscopically in the skin tissue and subcutaneous fat layer, as well as surrounding soft tissues: fullness, interstitial tissue swelling, dystrophic and necrotic changes, and sharp infiltration of resident macrophages in this area. Steatonecrosis with multiple foci, focal fullness and interstitial tumor foci are detected mainly in the surrounding tissue of the skin and adipose tissue. Inflammation is essentially a response of the vascular and mesenchymal tissues in the affected tissue area. In our work, the damage of cell components caused by inflammatory factors continues with the development of paranecrosis, necrobiosis, and necrosis. In particular, the vascular response that occurred in the surroundings of the affected tissue in 1 day, the degranulation of fat cells under the influence of leukotrienes (pro-inflammatory mediators) released by necrotic cells, leads to the rapid development of the alteration process in the surrounding tissues, and this, in turn, occurs with the emergence of secondary alteration. The changes that occurred in 1 day are mainly manifested by the involvement of vascular components in the process, tissue hypoxia, and the development of dystrophic-necrotic changes. Over time, plasmorrhagia, leukodiapedesis and migration of many neutrophils are observed in the damaged area. These changes are clinically manifested by the development of swelling, redness, increased local temperature, pain, and a dysfunctional state in the affected area. In laboratory indicators, it is mainly manifested in the form of leukocytosis, neutrophilia. As a result, the formation of many inflammatory infiltrates in the skin leads to a sharp violation of blood circulation and lymph drainage function in this area, a sharp increase in the rheological properties of blood in the vein and the occurrence of a sludge phenomenon in small capillaries, a sharp derailment of metabolism in tissues, a large accumulation of intermediate metabolites, and a decrease in resistance to secondary infectious factors. it is explained by the low effectiveness of antibacterial therapy in the treatment of this disease. These changes develop more sharply and begin to spread to the surrounding tissues and lead to further

development of the secondary alteration process.

Micrographs of skin and subcutaneous adipose tissue perimeter areas and tissue samples from group 1 rats.

Research results and their discussion

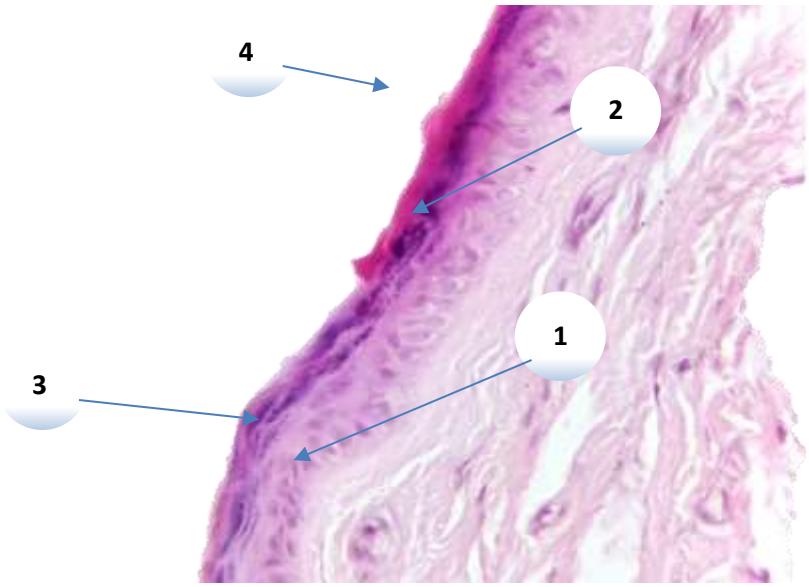

Figure 1. Group 1. The preparation contains white rat skin, intact skin. The epidermis does not have a shiny layer, so it consists of 4 layers: basal (1), spiny (2), granular (3) and horn (4) layers. Undoubtedly, the stratum corneum is thin: it consists of only 3-4 rows of freezing cells. As a result, the total thickness of the epidermis is very thin. Paint G-E.1

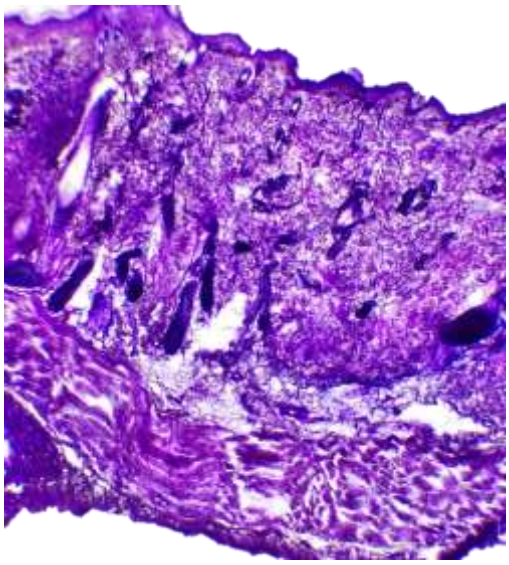

Figure 2. Group 1: White rat skin tissue in the preparation. The histioarchitectonics of the dermis is unchanged, between the hypodermis and muscle fascia, hematoma and sclerosis foci are almost undetectable. Dark arrows and follicles are unchanged. The size is 10x10. Paint Altsian blue.

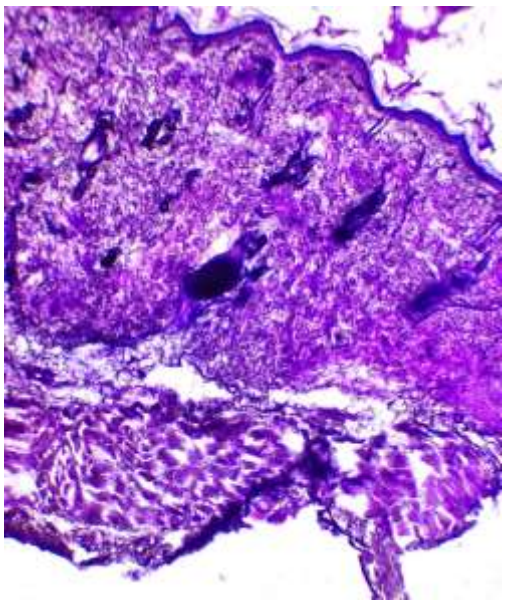

Figure 3. Group 1. White rat skin tissue in the preparation. In the dermis, without histioarchitectonic changes, interstitial swellings of various degrees are detected between the hypodermis and muscle fascia. The size is 10x10. Paint Altsian blue.

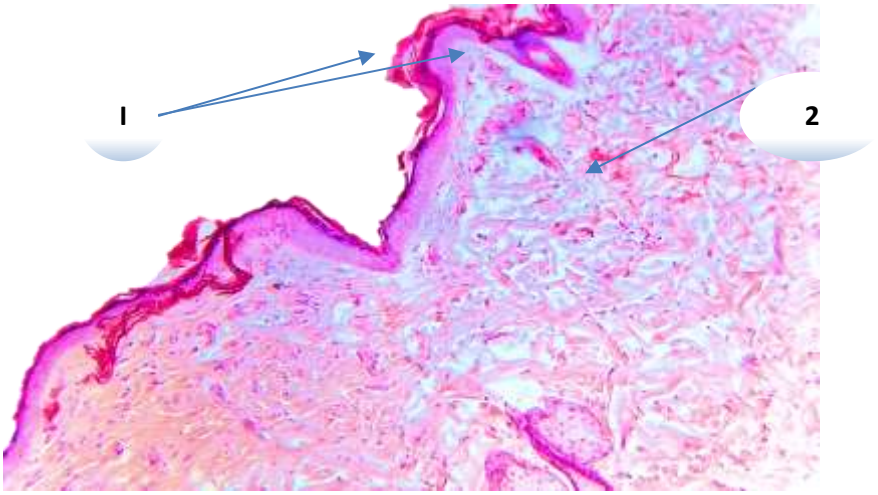

Figure 4. Group 1. The preparation contains white rat skin, intact skin. Dermis consists of two layers.

I. The papillary layer consists of connective tissue with deep papillae penetrating the epidermis (which expands the area of the growing layer of the epidermis) and non-porous connective tissue. II. Underneath lies the reticular layer, which is formed by loosely formed connective tissue. At the end, strong oxyphil bundles of collagen fibers moving in different directions and forming a three-dimensional network prevail. In addition, there is a network of elastic fibers. Of the skin derivatives, there are only sweat glands. Hairs and sebaceous glands were not detected. Paint G-E.10x4.

In the preparation, intact rat skin, skin and subcutaneous tissue, poorly developed fullness around the tissue, uneven interstitial edema, fibrous structures and other tissue components are detected.

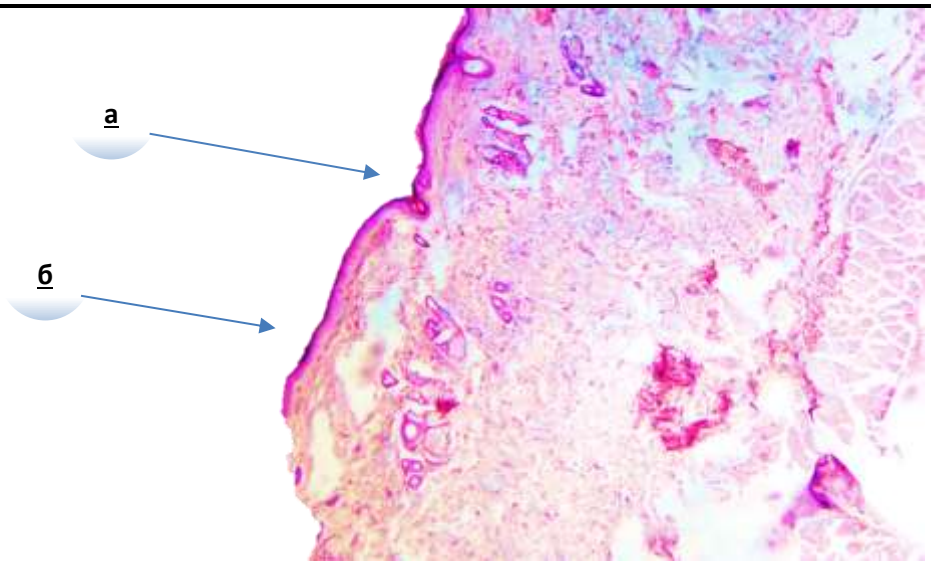

Figure 5. Group 1. Intact skin. The drug contains white rat skin (a- spiny layer, b- granular layer). Hair follicles are identified on the skin. Paint G-E.10x10

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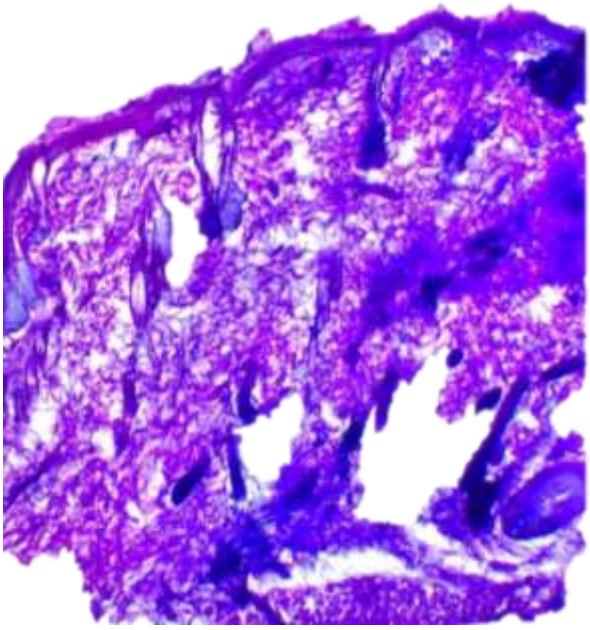

Figure 6. Group 1. White rat skin tissue in the preparation. In the dermis, without changes in histioarchitectonics, the foci of hemorrhage are not detected. Size 4x10. Paint Altsian blue.

General skin morphology and the wound healing process. In intact rat skin stained with hematoxylin and eosin, basal, spiny and granular layers are clearly visible in the homotopic area of the wound in experimental animals (Figures 1 and 2, a and b).

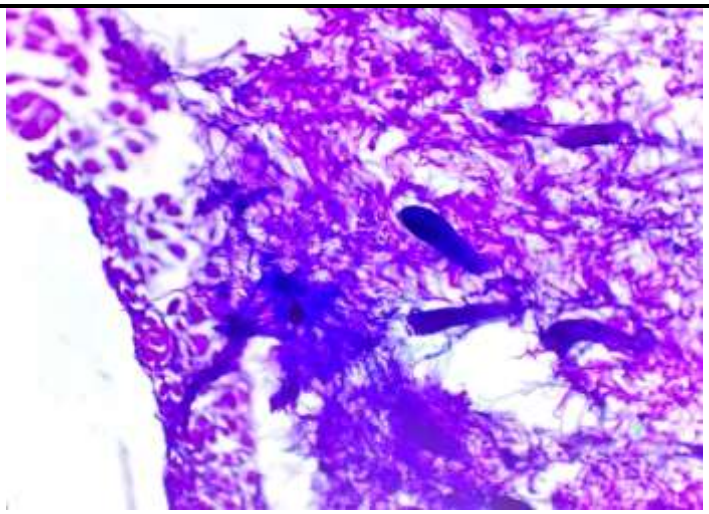

Figure 7. Group 1. White rat skin tissue in the preparation. Schiff positive structures (sour mucopolysaccharides) are detected in the dermis. Hematoma foci are not identified. The size is 10x10. Paint Altsian blue.

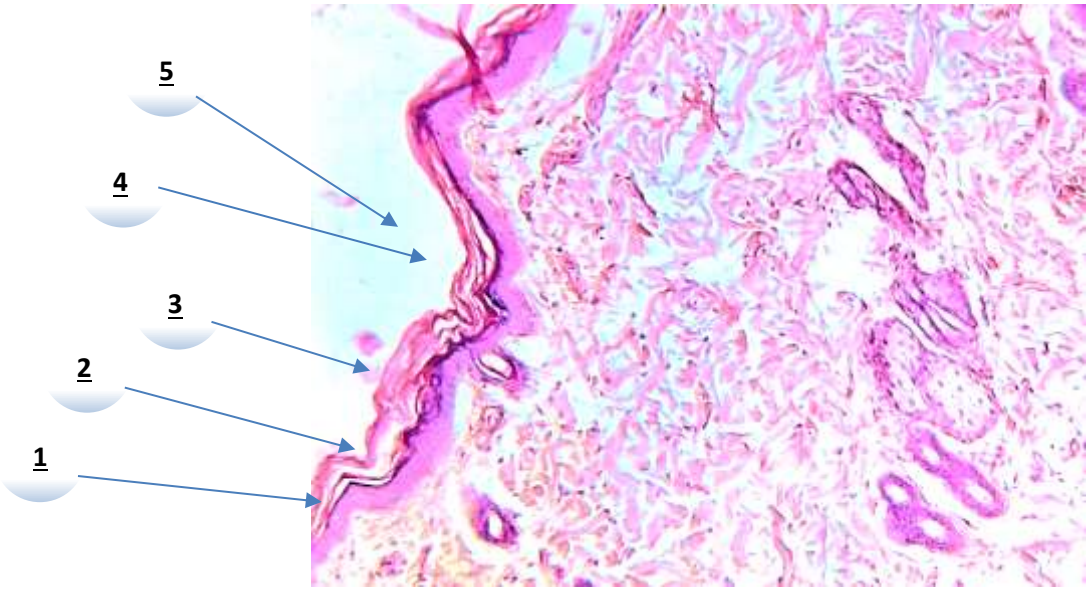

Figure 1. Group 2. White rat skin in the preparation. Intact skin. Epidermis consists of 5 layers: basal (1), spiny (2), granular (3), shiny (4) and horny (5) layers. The horn layer is slightly thickened compared to the above pictures. Paint G-E.10x10.

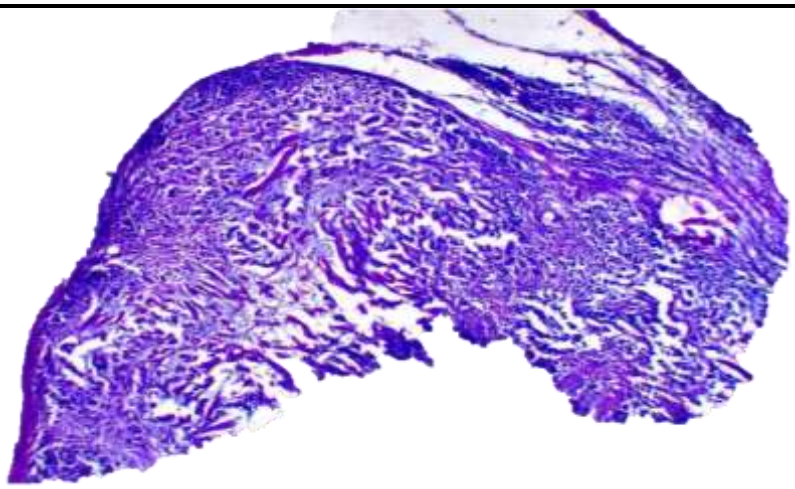

Figure 2. Group 2. Morphological appearance of hemostatic Bombyx mori fibroin-based fluff on the surface of white rat skin in the preparation. It contains collagen fiber structures. Paint Altsian blue. Size 4x10.

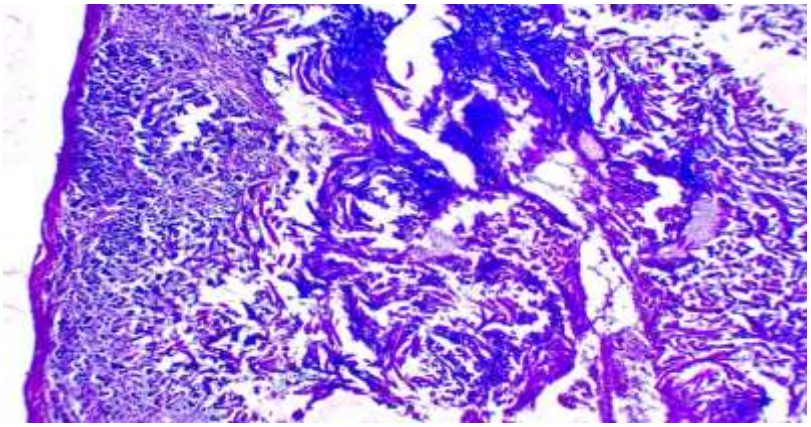

Figure 3. Group 2. Morphological appearance of hemostatic Bombyx mori fibroin-based fluff on the surface of white rat skin in the preparation. It contains collagen fiber structures and Schiff positive structures. Paint Altsian blue. The size is 10x10.

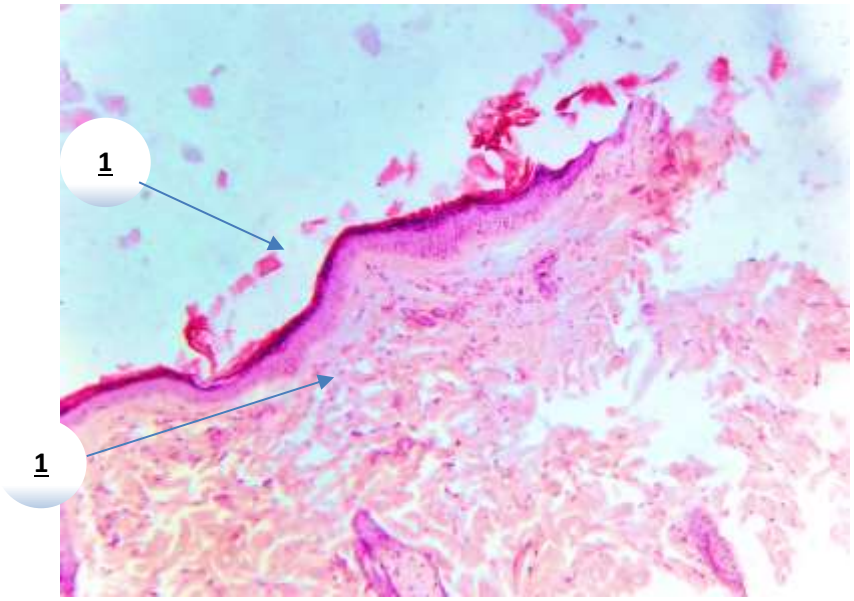

Figure 4. Group 2. White rat skin in the preparation. Intact skin. In the dermis layer, the papillary layer (1) is thinned, papillae are relatively weakly developed. Reticular layer (2) — unchanged. Paint G-E.10x10.

According to the measured area of the injury, it was not significantly different from group 1 in this period. The predominance of the alterative stage of inflammation and the destructive and dysregenerative changes of the stoma of the skin layers remained in the injured branches. It was found that around most of the foci of inflammation, a poorly formed neutrophilic infiltration and infiltration of a small number of lymphocytes and plasmocytes continued. Foci of coagulation necrosis are identified in the subcutaneous muscle layers. It is determined that healthy tissue components and uneven interstitial tumors are preserved in the stroma. Macroscopically, the cross section of the wound was significantly reduced, focal reepithelialization of the wound surface was detected in some rats of this group. Signs of uneven fullness are detected in blood vessels. Few migrating leukocytes are detected in perivascular areas. Reparative regeneration foci, proliferative active foci of mesenchymal cells are identified in most damaged skin structures. No significant signs of reparative regeneration were evident around the wound closed with gauze.

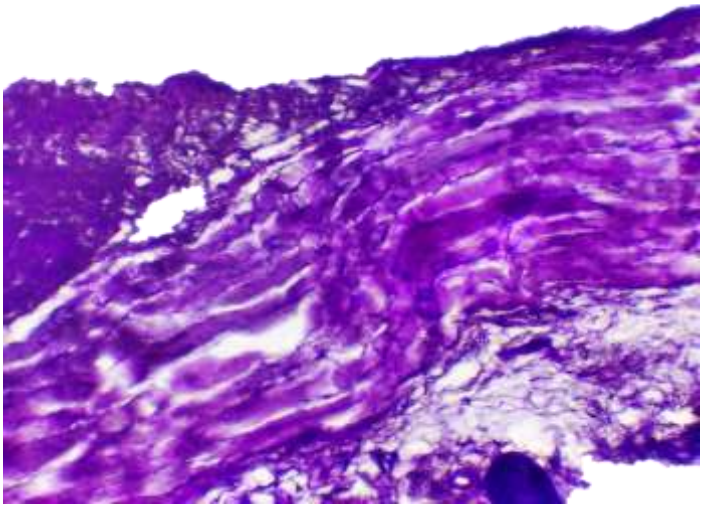

Figure 5. Group 2. White rat skin tissue in the preparation. Adipose tissue is preserved between the hypodermis and muscle tissue. In the muscle tissue, weakly formed intermediate tumor foci are identified. Paint Altsian blue. The size is 40x10.

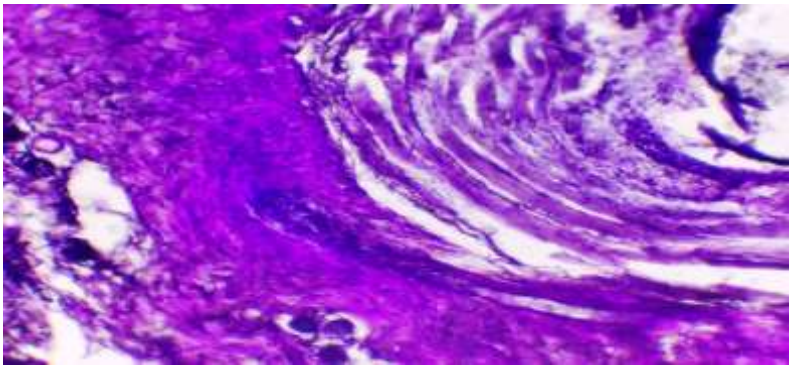

Figure 6. Group 2. White rat skin tissue in the preparation. Between the hypodermis and muscle tissue, intermediate foci of swelling are identified. Paint Altsian blue. The size is 40x10.

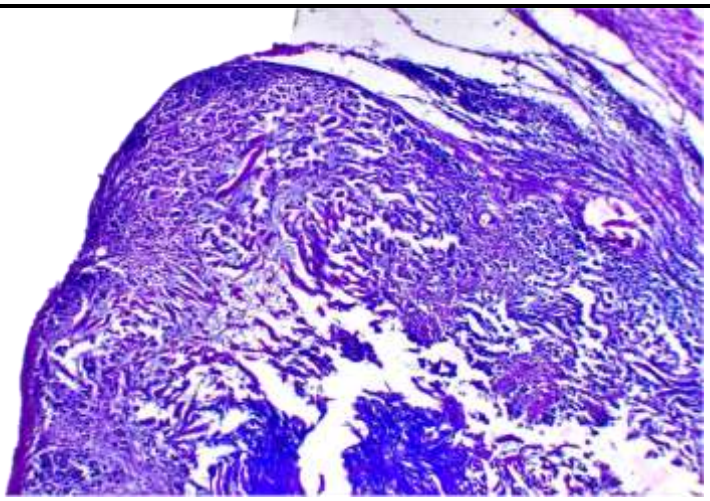

Figure 7. Group 2. White rat skin tissue in the preparation. Between the hypodermis and muscle tissue, intermediate foci of swelling are identified. Paint Altsian blue. The size is 40x10.

Summary:

1.In group 1 rats with diabetes induced in the skin tissue, it is determined that the reparative regeneration processes of the skin continue with the relatively slow formation of stepwise regeneration indicators, the increase of coarse fibrous granulation tissue structures around the wound, and the development of many defective foci at the edge of the wound.

2. In the 1st group, in the condition after conventional treatment, proliferatively active surfaces of various crater-like sizes on the edges of the flat epithelium around the wound, local hemosiderosis foci developed after the foci of point hemorrhage in the pit are determined. On the histological structure of the skin, foci of coagulation necrosis are identified mainly around the reticular and granular branches of the dermis rich in vessels.

3. So, summarizing the micrographs studied above, no significant changes in the speed of the reparative regeneration process of wounds covered with gauze were detected in rats with low exposure. The basal layer of the dermis continues with a sharp violation of epithelization in damaged areas and the appearance of defects of various sizes. This means that the fact that it leads to a medium-low acceleration of the effectiveness of treatment from a clinical morphological point of view cannot be a special basis for the rational use of bandage dox for the healing process of skin wounds.

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