the presence of mineral may change the nature of organization of collagen molecules in the fibril [15].

Mineral crystals located in the intrafibrillar spaces have a Lamellar form and dimensions correlating well with reported data [11, 15]. The form differences between the intra- and extrafibrillar crystals are probably associated with the dissimilar mechanisms of their nucleation and growth in these parts of the bone matrix [8].

The investigation conducted has provided evidence of the presence of a microcanalicular system forming a network in bone matrix. Its functional significance may be assumed to lie in increasing the surface available for ion exchange between the mineral and the "bone fluid." The main routes for fluid circulation are precisely along the edge of mineralized matrix forming the walls of the bone lacunae and canaliculi, whereas the flow is diminished close to the osteocytes and their processes [13]

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Morphological Substantiation of the Choice of Composition and Structure of a Sodium Alginate-Based Biologically Active Composition for Healing Wounds

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In conection with the appearance of a large number of novel biologically active compositions (BAC) for healing wounds in recent years, the substantiation of the choice of their composition and structure is very urgent [1, 2, 4]. The efficiency of BAC based on sodium alginate in treationg experimental suppurating wounds was shown earlier [3] Nevertheless, the problem of choosing the best makeup and structure of such a composition remains open, and the present article is devoted to this topic.

MATERIAL AND METHODS

We studied models of suppurating wounds in 88 white nonpedigree single-sex rats weighing 180-200 g. After depilation and antiseptic treatment, a skin section 2.5 cm in diameter was resected on the animals'

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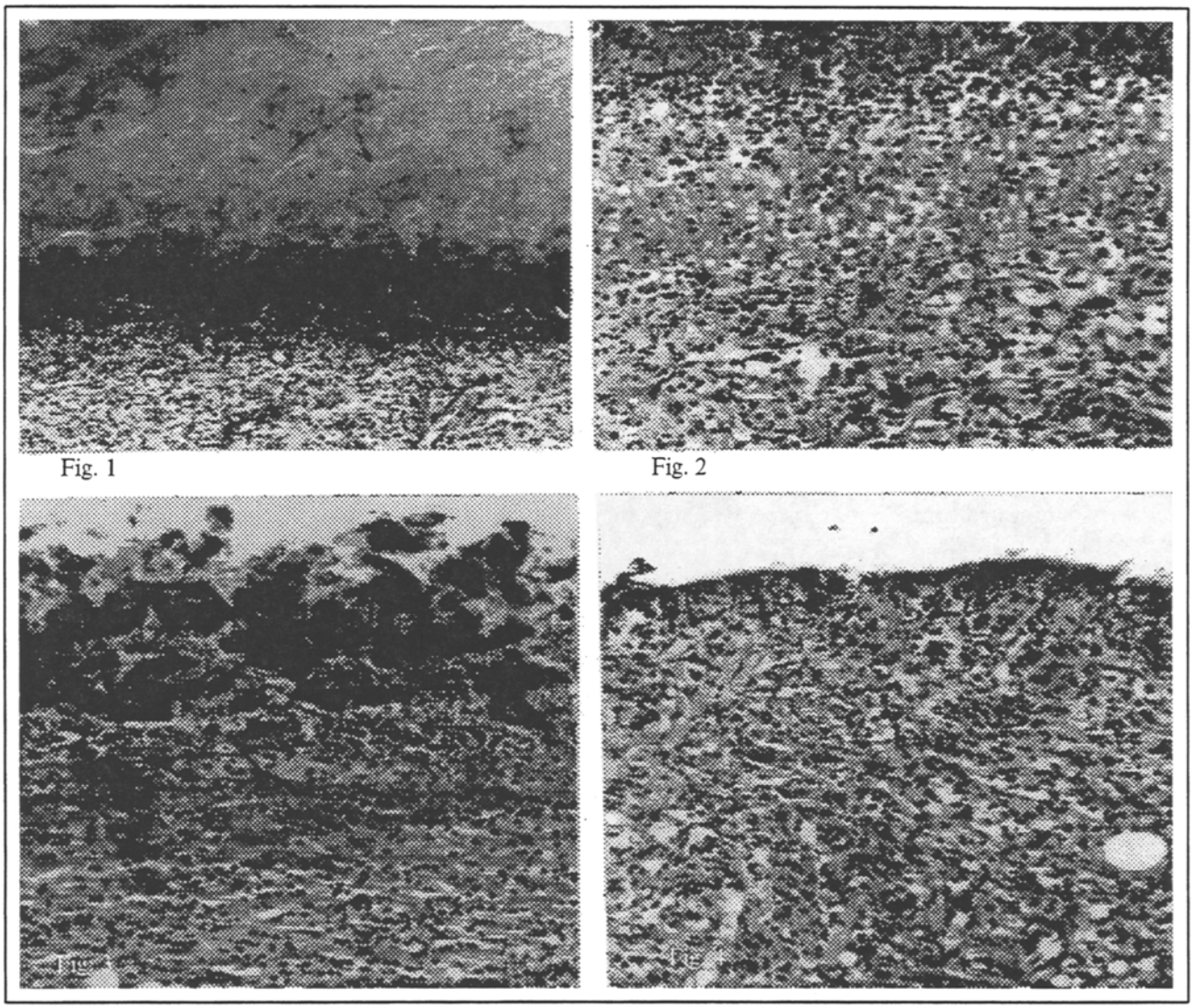

Fig. 1

Fig. 2

Fig. 1. Placebo. Sodium alginate, 7th day. Thick layer of suppurative and necrotic deposits on wound bottom. Stained with hematoxylin-eosin, 90x.
Fig. 2. Sodium alginate with sizomicin , 7th day.The wound bottom is covered with a dense layer of suppurative and necrotic deposits. The underlying granulation tissue exhibits insignificant infiltration. No edema. Stained with hematoxylin-eosin, 160x.
Fig. 3. Sodium alginate with protease C, 3rd day. Loosening of suppurative and necrotic layer on wound bottom after application of BAC containing protease C. Stained with hematoxylin-eosin, 160x.
Fig. 4. BAC (125), 7th day. Wound bottom after healing with BAC (3 rebandagings) in matured granulation tissue with high collagen content. The wound surface is clean. Inflammation is absent in the deep layers. Stained with hematoxylin-eosin, 160x.

backs under ether narcosis to the underlying fascia. The wounds were left under a crust without bandages for fixing their edges and forming granulation tissue. In two or three days, the crust was removed, the bottom of the wound was incised slightly with a blade to obtain sections of ischemic necrosis, and then 10^9 microbial bodies of a 24-hour culture of *Ps. aeruginosa* were introduced into the wound. In three days, application of the BAC to the formed suppurating wounds was commenced. Two series of experiments were run. The first was aimed at finding the optimal BAC composition by morphological investigation of the reperative preocesses in the model wounds. All the animals were divided into four groups of 15 each. A sodium alginate powder without biologically active substances was applied to the wounds of the rats of group 1 (control). The wounds of groups 2 and 3 were treated with a sodium alginate powder containing 1% sizomicin and 0.25% protease C, respectively. A BAC containing all the above components was applied to the wounds of the group 4 rats. All the preparations employed in the first series of experiments were a finely dispersed powder with particles 125 in diameter and containing 24% calcium gluconate.

The second series of experiments was aimed at morphological detailing of the most suitable size of the BAC granules and their content of calcium gluconate, whose addition to the alginate retards its degradation in

the wound contents and may affect the proteolytic activity of the enzyme introduced into the BAC. A BAC with a granule diameter of 315 and 600 , respectively was applied to the wounds of 14 animals of groups 5 and 6. The effect of a powder containing calcium gluconate (12 and 48%, respectively) on the wound process was studied in groups 7 and 8 (14 rats). Indications of inflammation and the presence or absence of necrotic detritus and granulations were watched for in the daily rebandagings. Bacteriological investigations were performed. On the 3rd, 5th, 7th, and 9th days, pieces of tissue up to 3 mm thick were embedded in paraffin. Histological sections 7 thick were stained with hematoxylin-eosin and picrofuchsin.

RESULTS

All the wounds before treatment were suppurating sources with a moderate secretion coating of a turquoise-gray color with a characteristic odor. The surrounding skin was edematous and hyperemic. The initial semination was 3.8 10^6 microbial bodies (m.b.) per cm^2 of wound surface.

The group 1 animals retained for a long time inflammation and a necrotic coating firmly fixed to the underlying granulation tissue. The wounds became clean on the 11th or 12th day. By this time, their semination virtually did not change and was 2.1 x 10^6 m.b.cm^{-2}. Histologically from the 3rd to the 9th day, the bottom of the wounds was formed by maturing granulation tissue with moderate edema and inflammation covered with a tick coat of necrotic detritus with microbe colonies firmly fixed to the granulations (Fig. 1).

In the group 2 animals, a necrotic coating was observed for a long time (up to the 7th to 9th day) on the wounds, but the inflammatory phenomena vanished quite rapidly, on the 5th to 7th day. Semination of the wounds on the 7th day was 3.8 x 10^4 m.b.cm^{-2}. In the histological preparations, notwithstanding the thick layer of suppurative and necrotic deposits on the surface of a granulation, inflammatory phenomena were practically absent by the 7th day (Fig. 2), which we attribute to the pronounced antibacterial activity of the given BAC.

In the group 3 animals, unlike those of the first two groups, the wounds became free of suppurative and necrotic deposits on the 5th day, after which they became covered with succulent pink granulations. At the same time, the semination of the wounds with microbia; flora remained at a high level and on the 5th day was 4.3 x 10^6 m.b.cm^{-2}. Microscopic examination of the wound bottom sections on the 3rd day revealed loosening og the suppurative and necrotic detritus (Fig. 3), and on the 5th day separation thereof, with cleaning of the wound surface, which was presumed to be due to the effect of the protease. The fact that on just the 5th day a considerable number of collagen fibers were observed in the granulation tissue attracted attention. This reflected the general trend of the wounds toward earlier maturing and fibrous tissue formation on their bottom in comparison with the control group of animals.

The distinctive features of the antimicrobial and necrolytic substances on the wounds were most manifest when BAC containing both these components were applied. For example, cleaning of the wounds with diminishing inflammation in the surrounding tissues was observed as soon as in the 3rd to 5th day. The semination of the wounds by this time dropped to 3.8 x 10^5 m.b.cm^{-2}. Histologically, by the 5th day the bottom of the wounds was represented by granulation tissue with an insignificant thickness of the suppurative exudate coating, without features of inflammation (Fig. 4). The 7th day saw further maturing of the granulations and transition of the wound process to the cicatrization stage. A large number of collagen fibers was found in the deep layers of the bottom of the wounds. This reflected active synthesizing processes in the newly formed tissue.

In the second series of experiments, the clinical and morphological picture of the wound process for application of BAC-315 was the same as for a BAC with a granule diameter of 125 ц, as described for the first series of experiments (group 4.) No clinical differences were found either in the group of animals to whose wounds BAC-600 was applied. At the same time, the wounds of these animals6 which became clean by the 7th day, morphologically appeared to be "drier" and contained a larger amount of newly synthesized collagen. This may be due to the higher sorption activity of the BAC with the given structure. On the other hand, it was easier to apply a powder with a smaller granule diameter to the wounds, and it adhered better to their surface than the coarser one.

In the experiments with a BAC containing different amounts of calcium gluconate, we observed no noticeable differences in the clinical and morphological features of repair. Nevertheless, with less calcium the BAC was more liable to destruction, which releases biologically active substances into the wound medium more rapidly than a BAC containing 48% calcium, which preserved its structure for a longer time.

Hence, our studies indicate the expediency of employing a biologically active composition with a polyfunctional effect for healing suppurative wounds in the first phase of the wound process. The biologically active substances (sizomicin and protease) eliminate the etiopathogenic factors of suppurative inflammation - necrotic tissues and microbial bodies, while the polysaccharide basis of the preparation stimulated repair processes and prepares the wound for cicatrization. Our observations show that it is best to employ a biologically active composition with a granule size of

315 μ and containing 24% calcium gluconate. These conclusions were subsequently confirmed by clinical observations.

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Experimental Estimation of the Effectiveness of Different Antiadhesion Remedies

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Numerous studies have been made of the etiopathogenesis of the postoperative formation of adhesions [2]. Numerous methods and preventive measures have been developed and proposed, but they failed in most cases. The problem of postoperative adhesions in gynecologic reconstructive plastic surgery is especially serious due to the need to restore the anatomic-functional mutual arrangement of the ovaries and uterine tubes, which determines the effectiveness of these interventions.

Different models of reconstructive operations on animals are employed which make it possible to estimate the efficacy of the methods and means suggested. Recently a variety of soluble polymers and preparations of biological origin were suggested for the prevention of postoperative adhesions [2-4].

TABLE 1. Comparison of Suture Adhesions of Parietal Peritoneum of Lateral Abdominal Wall of Rat after FG-1 and TS-7 Use (M±m, n=10).

group	prevalence of adhesions	type	density of adhesions	total number
1. FG-1	1,6±0,4	1,0±0,3	1,6±0,3	4,2±1,0
2. FS-7	1,8±0,5	1,2±0,4	1,4±0,3	4,4±1,2
3. Control	3,0±0,3	3,2±0,3	2,3±0,4	8,5±1,0
	P_{1-2}>0,05	P_{1-2}>0,05	P>0,05	P_{1-2}>0,05
	P_{1-3}<0,02	P_{1-3}<0,001		P_{1-2}<0,01
	P_{2-3}<0,05			P_{2-3}<0,02

The purpose of the present work was to study the effectiveness of fibrin glue (FG-1) as well as interseed (TS-7), a resorbed "barrier" of oxidized and reduced cellulose (Johnson & Johnson, USA) on models of the formation of adhesions in rats.

MATERIAL AND METHODS

Fifteen albino breedless rats weighing 180-200 g were used in 30 experiments. Fibrin glue FG-1 was used in the first group (10 experiments). Interseed TS-7 was used in the second group of 10 experiments and no supportive remedies were employed in 10 experiments of the third group, which served for a model of the formation of adhesions in the abdominal cavity. The operations were carried out under general anesthesia by intramuscular injection of hexenal at a rate of 100 mg per kg. The abdominal cavity was dissected by medial incision, after which the lateral abdominal wall evaginated by a special device and the parietal peritoneum was exposed. A 1x3 cm flap of the parietal peritoneum of the lateral abdominal wall was dissected. After that 10 nodal sutures were performed with catgut 30, using an atraumatic needle. This bilateral surgical intervention served as a model of the formation of adhesions in rats. When using supportive measures to prevent the postoperative formation of adhesions, the suture was covered either with fibrin glue to create a flat

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