animals with tumors that were fed bioginseng (Table 2). Thus, bioginseng normalizes the blood estradiol level, this possibly being one more mechanism explaining mammary carcinogenesis inhibition by this drug.

Our finding demonstrate a new indication for the use of bioginseng tincture: it can be used for the primary prophylaxis of mammary carcinoma. Breast cancer is the most prevalent oncologic disease in women [3]. Antiestrogens, recommended for the prevention of mammary carcinoma, induce a number of noticeable side effects [3,12].

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MORPHOLOGY AND PATHMORPHOLOGY

Peculiarities of the Relief of the Mineralized Surface of Lacunae and Canaliculi in Lamellar Bone

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The term "bone fluid," whose circulation is observed mainly in the lacunar-canalicular system, is used at present in a number of morphological and physiological investigations of bone. In fact, the term is used to designate an interstitial fluid of bone which differs from blood plasma in its composition [4]. According to the Arnold-Frost model [7], during the blood-and-bone exchange the phenomenon of "bone fluid" filtration through the mineralized matrix is of prime importance. The extremely large surface of bone mineral crystals, even with a comparatively low flow of the fluid, provides a quick and effective equilibration of the Ca^{2+} and phosphate concentrations between the fluid and the mineral [6]. To determine the nature of the circulation processes in the mineralized bone matrix the microcorrosion method [2, 5] and various markers are used [6].

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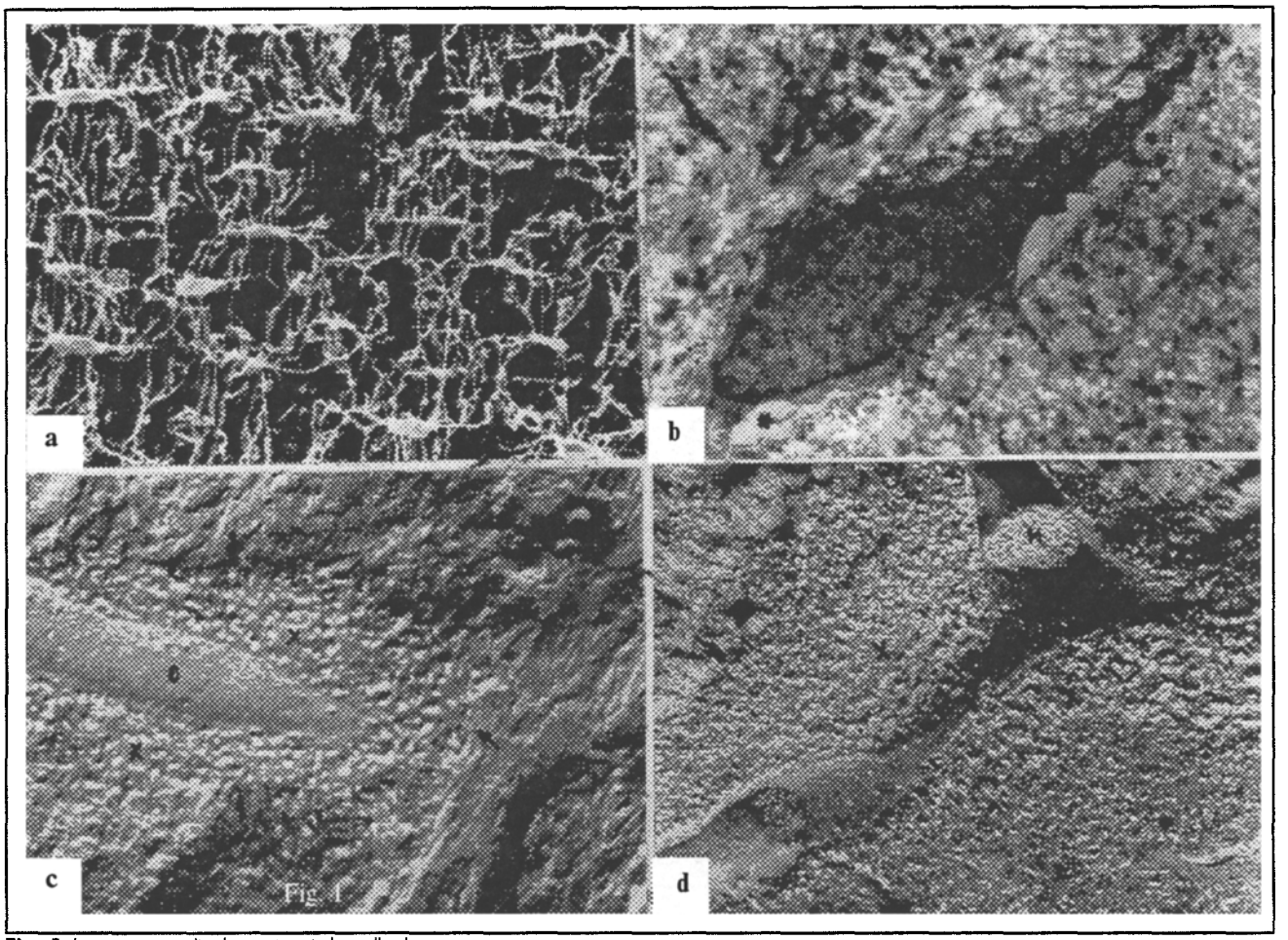

Fig. 1. Lacunar-canalicular system in lamellar bone.
a) spatial organization of lacunar-canalicular system in human parietal bone. SEM. 625x; b) osteocyte in bone lacuna. Asterisk marks pericellular space. TEM. 5000x; c) retinal substance (cross) between osteocyte process (circle) and bone canaliculi mineralized wall (arrow). Cryofractography. TEM. 100,000x; d) microfilaments (m) on osteocyte process split; cross: reticular substance; arrow: wall of bone canaliculi. Cryofractography. TEM. 50,000x.

The peculiarities of the lacunar-canalicular spatial organization of the compact and spongy substance of different human bones have been demonstrated recently [2, 5]. However, the interrelations and differences between micropores and the lacunar-canalicular system in bone matrix should be determined more precisely for a better understanding of fluid flow mechanisms in bone [9]. Indications of micropore presence were obtained during a study of double replicas of bone splits [14] and by the mercury porometry method [3]. A morphological analysis of these structures and of their interrelations with the bone canaliculi lumens has not been presented. The details of the relief of the bone lacuna and canaliculi mineralization front Have hardly been investigated to date, although it is supposed that the composition and structure of perilacunar and pericanalicular bone exhibit a certain specificity [12].

The aim of this study was to investigate a mineralization front relief of the bone lacunar and canalicular walls after removal of the organic phase of bone.

MATERIAL AND METHODS

Samples of human parietal bone and femur compact substance (subjects aged 19-44 years) were investigated. Cases of osteoarticular apparatus diseases were excluded. The samples of native bone and bone deorganified by sodium hypochlorite [1] were studied after routine preparation by the SEM and TEM methods. Additionally, freeze-fracturing of the samples was carried out with a BAF-400D instrument (Balzers), followed by platinum and carbon application on the split surface. The replicas obtained were studied under an EM-420 microscope (Philips). For preparation of the microcoroosive preparations of the lacunar-canalicular system the bone samples were saturated under low pressure with methylmetacrylate. After polymerization the bone organic component was removed in 5% sodium hypochlorite solution, after which demineralization was performed in 3% HCl. The specimens prepared were frosen in supercooled liquid nitrogen and dried on FDU-10T apparatus (Balzers), followed by copper dusting in argon on SCD-040 apparatus (Balzers). The preparations were examined under a SEM-515 microscope (Philips).

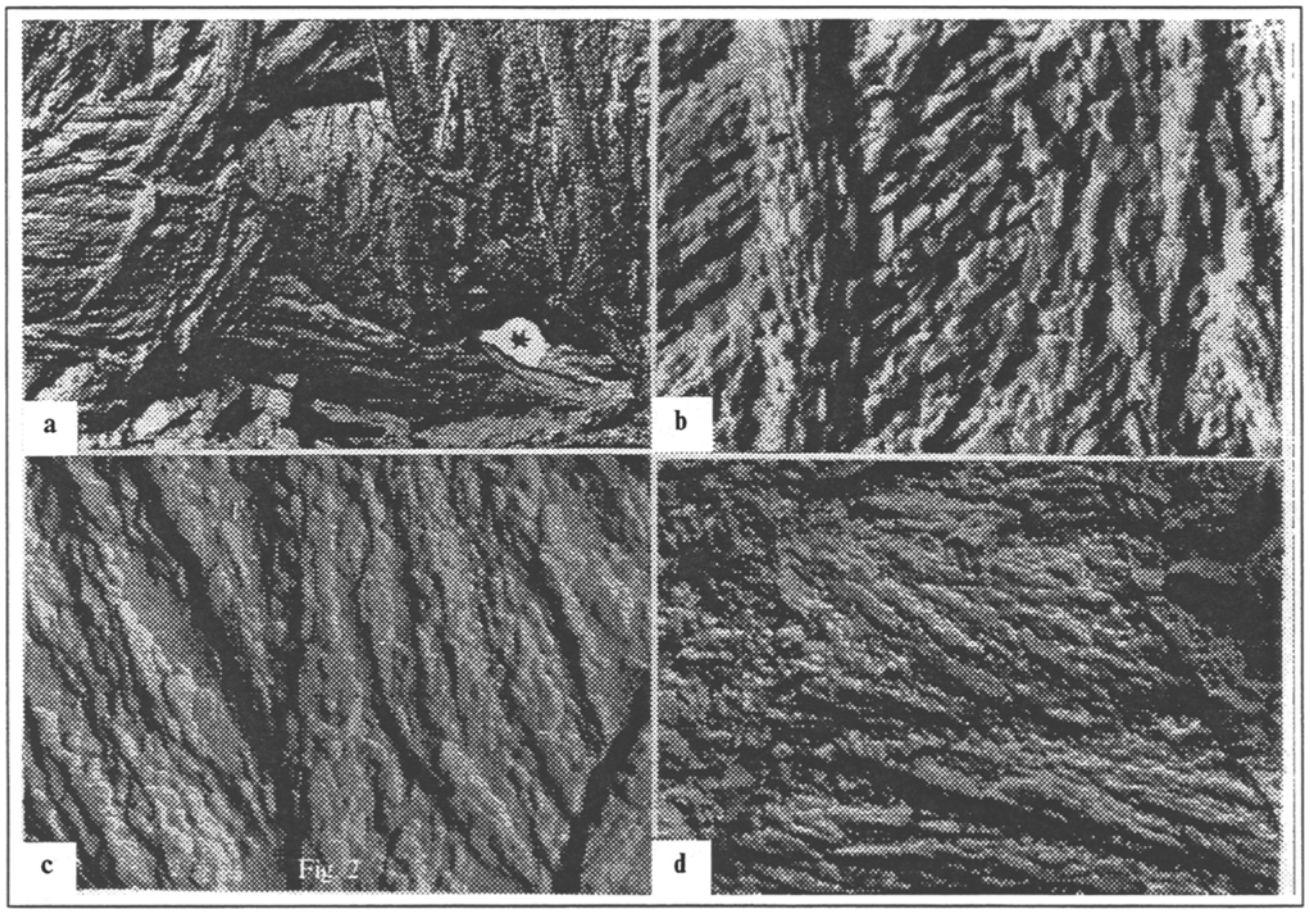

Fig. 2. Peculiarities of relief of mineralized surface of bone lacunae and canaliculi.
a) relief of mineralization front of bone lacuna bottom. Asterisk marks ostium openings of canaliculi. Cryofractography. TEM. 20,000x; b) crystals of rod-shape (arrow) and plate-shape (double arrow) in the bone lacuna wall. Cryofractography. TEM. 100,000x; c) lamellar crystals in mineralized basal substance covering collagen fibrils. Cryofractography. TEM. 100,000x; d) ostium openings of bone microcanaliculi in wall of bone canaliculi. Cryofractography. TEM. 100,000x.

RESULTS

A great number of lacunae connected by a developed network of bone canaliculi (Fig. 1, a) were shown to be present. The structure of the lacunae and canaliculi is characterized by high variability and complexity. The median dimensions of the lacunae are 7x10x18 μ and the distance between two adjacent lacunae commonly varies in the limits of 25-35 μ. One lacuna may have up to 50 canaliculi forming a dense network in the bone matrix.

Osteocytes do not fill the whole volume of the lacuna and are separated from the walls by the extracellular space, where scattered nonmineralized collagen fibrils are situated (Fig. 1, b). The width of this space depends on the functional state of the cell and may change during its life activity. Bone canaliculi coming from the lacunae frequently curve and the width of their lumen somewhat varies. A canaliculus section has a rounded, oval, or triangular form. Osteocyte processes are located in the central parts of the canaliculi, although they may approach the walls as they run their course. The canalicular wall is formed by collagen fibrils that sometimes project into the lumen.

The osmiophilic line demarcating the bone matrix from the canalicular lumen is distinctly seen on demineralized preparations.

The osteocyte processes are separated from the mineralized bone matrix by a layer of substance with a reticular structure (Fig. 1, c). This layer somewhat broadens at the sites where the cell processes divide. The processes contain separate vesicles, ribosomes, and microfilaments (Fig. 1, d). at some sites on the surface of the processes vesicle formation is determioned in the space between the processes and the canalicular wall.

Analysis of the data permitted us to determine the peculiarities of the mineralized surface of bone lacunae and canalicular relief. Thus, the surface of the walls of formed bone lacunae is made of mineralized collagen fibers of various thickness and of separately lying and variously directed collagen fibrils. Ostial parts of bone canaliculi are located in the funnel-like hollows between the fibers. Bone mineral crustals are distinctly seen on the surface of the collagen structures and in their spaces (Fig. 2, a). They are generally situated in layers, closely adjoining each other. The crystals revealed in the fibrils coming from the lacuna bottom have an elongated form

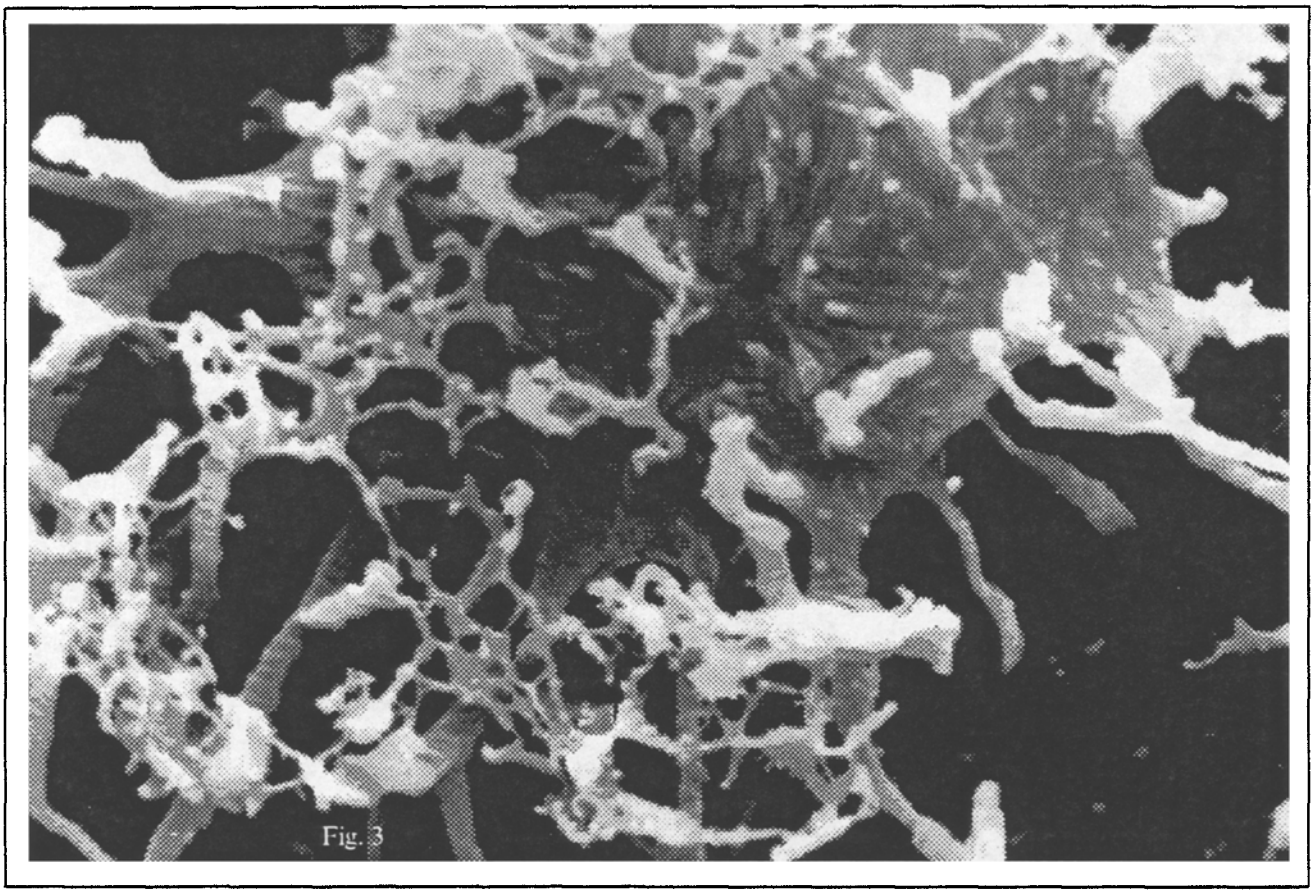

Fig. 3. Network of microcanaliculi (arrow) in bone matrix. Asterisk marks bone lacuna. SEM. 5000x.

and the following dimensions: (4-6)x(5-10)x(30-45) nm. They are arranged in the form of chains. The longtitudinal axis of such crystals is oriented at a small angle to the fibril direction in such a way that the crystal chains have an extended spiral structure (Fig. 2, b). Sometimes a few crystals in the form of polugonal plates with a maximum size of 50 nm can be seen on the fibrils' surface. In the interfibrillar spaces the crystals as a rule are lamellar and do not exceed 100 nm in size. Structures of (4-6)x(20-40) x(35-50) nm are seen more often. The crystals are arranged parallel to the bone lacuna surface or at a small angle. If the lacuna walls are covered with a bazal mineralized substance layer, then a significant number of lamellar crystals are seen on the fibril surface or they may cover the whole surface of the fibril (Fig. 2, c). In this case the crystals are closely adjoined to each other or are overlap like tiles.

The study of the relief of mineralized bone canaliculi shows a spiral arrangement of the mineralized collagen fibrils at sites of their connection with the bone lacuna. The spiral turn may be diverse and the fibril localization in this region varies from practically longitudinal to almost transverse. Moving away from the lacuna, the collagen fibrils are always oriented transversely vis-a-vis the canaliculi. Rod- or plate-shaped mineral crystals are detected on the fibril surface. Their ratio may significantly change at different sites.

Small openings 20-50 nm in diameter are revealed in some regions of the lacunar and canalicular surface (Fig. 2, d), their number varying in wide limits. The openings are more often seen in the interfibbrillar spaces and are much rarer on the surface of the mineralized collagen fibrils. They may be arranged in rows or be separately in the spaces between the crystals. Analogous openings are found on the splits in the matrix surrounding the lacunae and canaliculi. This indicates the presence of a system of microcanaliculi that may be revealed upon analysis of the microcorrosive preparations (Fig. 3). The microcanaliculi have no preferential direction, being sinuous and of unequal thickness. They are often branched and anastomosed, forming a network.

The present investigation thus demonstrated that the wall surface of the bone lacunae and canaliculi is formed of mineralized fibrils. The rod-shaped mineral crystals are arranged in elongated spiral chains. This spatial organization of the crystals corresponds to the location of the microfibrils having a spiral course in the collagen fibril. The size of the intrafibrillar crystals is practically the same as that reported by Glimcher [8] and is close to the lacuna size in a collagen fibril of 35.0-41.4 nm length and 1.5-3.0 nm diameter [10, 15]. This indicates the theoretical possibility of rod-shaped crystals localization in such regions. Besides,

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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