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SURGICAL SUTURE MATERIALS WITH SPECIAL PROPERTIES

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New approaches and technologies for structural and physical modification of surgical threads that were aimed at increasing the biocompatibility and suture reliability; decreasing tissue injury, rigidness, and wicking; and improving the manipulative properties were developed. The principles for producing fibrous polypropylene and polycaproamide suture materials with prolonged antimicrobial activity by binding chemotherapy drugs using ionic bonds were found. Groups of different reactivity in the fibers and drugs made it possible to control the duration and efficacy of their biological activity.

The principal function of any surgical suture is to guarantee a sufficiently tight, hermetic, and reliable connection of the sutured tissues and to hold them in a fixed position until the wound is healed [1, 2].

Sutures frequently serve no useful purpose after the edges of the wound have merged so that the foreign material should be removed by timely excision of the sutures or, more preferably, by biodegradation and resorption of the surgical threads [3, 4].

However, sutures should guarantee the reliable connection of synthetic prostheses and biological tissues for a very long time, i.e., the surgical threads must be bioresistant, during operations with organs and tissues in cardiovascular, plastic, and other types of surgery. Antimicrobial and other biologically active threads should be used in several surgical situations [5-7].

Surgical threads should be considered microprostheses that are implanted into tissues [8]. Therefore, the development and use of surgical suture materials (SSM) results primarily in the use of biocompatible (i.e., fulfilling their functions *in vivo* for the required time without being damaged) polymers [9-12]. Polymers used mainly to produce non-resorbable threads can be placed in the following order of decreasing biocompatibility [9, 13]: polytetrafluoroethylene (PTFE), poly(vinylidene fluoride) (PVDF), polypropylene (PP), polyethyleneterephthalate (PETP), and polycaproamide (PCA).

Recently, especially strong biocompatible threads (Spectra, Dyneema) of ultra-high-molecular-weight polyethylene that are prepared by gel technology have begun to be used in orthopedic surgery and traumatology [3].

Synthetic resorbable suture materials are threads of glycolic acid and *n*-polydioxanone copolymers in addition to their copolymers with ε-caprolactone, lactic acid, and trimethylenecarbonate in various combinations [14]. Resorbable SSM threads characteristically have identical biocompatibilities.

A rough and uneven scar forms from a pronounced tissue reaction to SSM and inflammations.

Surgical thread should have certain physicomechanical properties in order to fulfill its functions [8, 15]. These are an even thickness, high tensile strength including at a damp knot, the optimum relative elongation, sufficient flexibility, low shrinkage and creep, and frictional properties that provide reliable retention of the surgical knot but little injury on passage through the tissue.

The reduced strength of resorbable SSM during wound healing should be synchronized with the increased strength of the regenerated tissues.

The following requirements for surgical threads are also important to note. These are stable properties during prolonged storage under ordinary conditions, thread color that is distinguishable on the background of the wound, reproducible physicomechanical and medical-biological properties on going to the next production batch, stability to sterilization when packaged and reliable packaging, guaranteed sterility during storage, moderate cost, available raw material, and a finished product [3, 8].

The goal of the present work was to create scientifically justified and economically viable innovative technologies for industrial production of SSM with first-class, including new, medical and biological characteristics.

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Table 1. Effect of Heat-Treatment Conditions on Properties of PP Surgical Monothreads

Parameter	Starting monothreads	Monothreads heat treated without shrinkage	Monothreads heat treated with shrinkage			
			5%	10%	15%	20%
		Metric size EP 1				
Diameter, mm	0.110	0.113	0.116	0.118	0.120	0.122
Rigidity, cN·mm^2	2.9	2.6	2.4	1.8	1.4	1.0
Tensile strength at suture, N	3.5	5.7	5.5	5.6	5.7	5.7
		Metric size 1.5				
Diameter, mm	0.161	0.164	0.170	0.172	0.175	0.175
Rigidity, cN·mm^2	3.6	3.3	3.0	2.4	1.9	1.7
Tensile strength at suture, N	5.6	7.8	7.9	8.2	8.1	7.8
		Metric size 2				
Diameter, mm	0.234	0.236	0.240	0.245	0.247	0.249
Rigidity, cN·mm^2	4.5	4.2	3.7	2.8	2.2	2.0
Tensile strength at suture, N	13.4	17.3	17.4	17.7	18.2	17.6
		Metric size 3				
Diameter, mm	0.333	0.338	0.345	0.347	0.349	0.353
Rigidity, cN·mm^2	14.5	12.4	11.1	9.1	7.6	7.0
Tensile strength at suture, N	25.0	31.3	33.7	33.9	33.4	32.7
		Metric size 3.5				
Diameter, mm	0.370	0.376	0.387	0.398	0.415	0.430
Rigidity, cN·mm^2	18.6	15.8	15.1	14.7	14.0	13.0
Tensile strength at suture, N	38.2	47.3	50.2	49.5	50.0	46.4

PP SSM are highly biocompatible, have good strength parameters, are resistant to biodegradation, have a monolithic structure that prevents absorption of bacteria and infection of the sutures, pass without injury through tissues, and have a good cosmetic effect.

Technical PP monothreads that are manufactured domestically have insufficient strength at the knot, are rigid (initial elasticity modulus 8,000-9,000 MPa), and display hysteresis on winding. Structural modification could improve the strength and manipulation properties of PP monothreads.

Surgical PP monothreads are additionally heat treated at 140-165°C both without shrinkage and with shrinkage from 5 to 20% in order to produce monothreads with increased strength at the knot, the weakest link in the suture, and reduced rigidity as measured by the cantilever bending method (Table 1).

The additional heat treatment helps to improve the strength parameters at the knot. A temperature of 160°C is required for thread of the greatest diameter EP 3.5 (according to the European Pharmacopoeia) whereas 155°C is sufficient for threads of metric sizes EP 1 to EP 3. Heat treatment at such temperatures for 3 min provides increased strength at the knot and is most noticeable for thin monothreads.

The softest threads are produced with heat treatment and 20% shrinkage. The change of rigidity depends considerably on the thickness (the rigidity of EP 1 monothreads decreased by 65.5%; EP 3.5, by 30%). Shrinkage of 15% at 155°C should be considered to be optimal for improving the operational properties of EP 1 to EP 3 monothreads; 10% and 160°C, for EP 3.5.

Physical modification of twisted and braided PETP and PCA SSM was studied by forming bioresistant and hydrophobic SKF-26 fluoroelastomer polymer coatings.

Deposition of two successive coatings, the first of 5% and the second of 25% SKF-26 solution in Me_2CO, provided the most reliable surgical knot and a lack of wicking in the threads. The inter-fiber space was filled to the maximum by soaking with the 5% solution because of its low viscosity. Deposition of the 25% solution formed a thin shell on the surface that partially smoothed over the peaks and valleys and decreased tissue damage by the suturing material.

Phthalocyanine Blue (PCB) or Phthalocyanine Green (PCG) (12%) was added to the second polymer coating in order to create contrast on the background of the wound.

The coating reduced wicking to zero and helped to increase the reliability of the surgical knot (Table 2).

Post-operative wound infection remains one of the most important surgical problems. Therefore, production of antimicrobial fibers is a priority area for creating biologically active SSM because of the broad emergence of antibiotic-resistant or conditionally pathogenic microorganisms.

One of the most effective methods for introducing antimicrobial properties is modification of fibers by chemically binding biologically active compounds to them. Biological activity for 7-20 d is usually sufficient for SSM. This can be assured

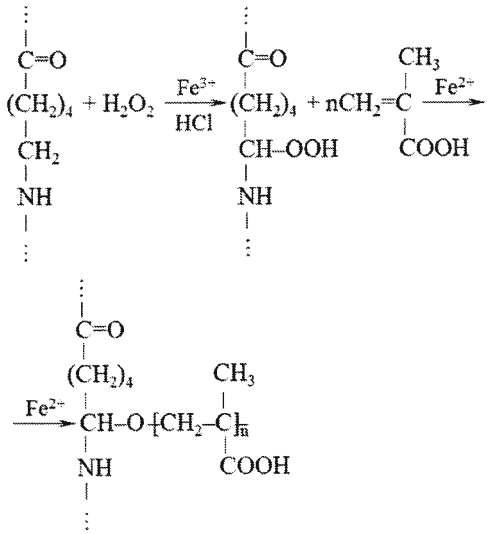
Table 2. Physicomechanical Properties of PCA and PETP Threads Coated with SKF-26

Number of coatings	SKF-26 solution concentration, %	Thread properties							
		diameter, mm	typical size, EP (USP)	thread polymer content, %	wicking, mm	knot reliability, %	bending rigidness, $cN \cdot mm^2$	knot tensile strength, N	knot fracture elongation, %
				PCA twisted threads					
0	0	0.342	3 (2/0)	0	120	70	0.37	20.7	28.2
1	5	0.338	3 (2/0)	7.48	0	58	n.d.*	21.3	42.0
1	25	0.334	3 (2/0)	18.6	0	80	n.d.	23.6	40.0
2	5 + 25	0.326	3 (2/0)	19.9	0	85	1.22	25.4	46.0
2	25 + 5	0.320	3 (2/0)	16.4	0	75	n.d.	28.8	45.3
3	5 + 25 + 5	0.315	3 (2/0)	18.4	0	80	n.d.	28.6	47.3
3	5 + 25dye + 5**	0.315	3 (2/0)	18.9	0	90	0.95	29.6	47.1
				PCA braided threads					
0	0	0.380	3.5 (0)	0	80	68	0.50	39.9	23.1
3	5 + 25dye + 5**	0.369	3.5 (0)	20.3	0	93	1.47	41.0	36.8
0	0	0.481	3.5 (0)	0	82	75	n.d.	52.4	25.5
3	5 + 25dye + 5***	0.466	3.5 (0)	22.2	0	95	n.d.	56.0	37.9
				PETP twisted threads					
0	0	0.331	3 (2/0)	0	34	40	0.36	26.8	28.5
1	5	0.327	3 (2/0)	9.3	0	20	n.d.	28.4	27.5
1	25	0.320	3 (2/0)	20.5	0	80	n.d.	28.4	28.3
2	5 + 25	0.315	3 (2/0)	21.4	0	85	0.99	29.0	26.7
2	25 + 5	0.310	3 (2/0)	21.0	0	75	n.d.	29.8	27.0
3	5 + 25 + 5	0.312	3 (2/0)	19.9	0	80	n.d.	30.4	28.5
3	5 + 25dye + 5***	0.312	3 (2/0)	19.9	0	90	0.96	30.6	28.3
				PETP braided threads					
0	0	0.333	3 (2/0)	0	27	40	0.48	28.3	20.0
3	5 + 25dye + 5***	0.316	3 (2/0)	20.2	0	85	1.26	30.1	30.3
0	0	0.470	4 (1)	0	33	40	n.d.	48.0	35.0
3	5 + 25dye + 5***	0.455	4 (1)	18.9	0	85	n.d.	49.8	36.5

*n.d., not determined; **dye = PCB dye; ***dye = FCG dye.

by binding the active ingredient using ionic bonds. Naturally, the drugs and fibers should contain the appropriate ionizable groups.

Carboxylate-containing PCA threads were produced by grafting methacrylic acid (MAA), which was initiated by the Fe^{2+}–H_2O redox system. One system component was converted beforehand to a peroxide or hydroperoxide by successive treatment with $FeCl_3$ in dilute HCl and aqueous H_2O_2 solution in order to suppress the homopolymerization reaction:



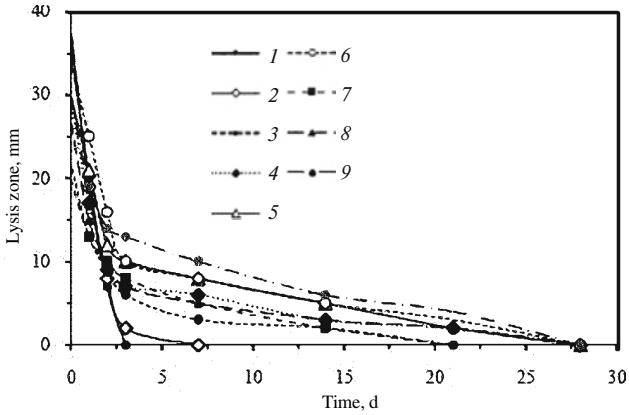


Fig. 1.

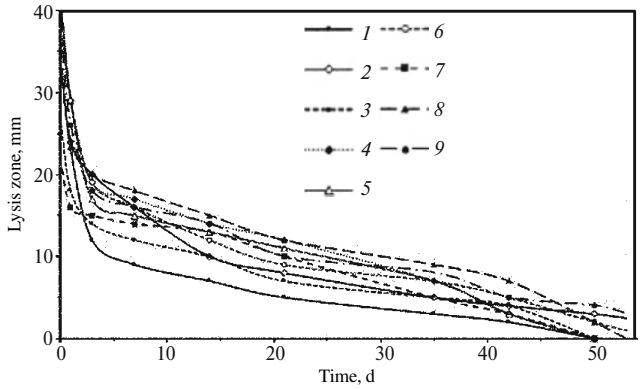


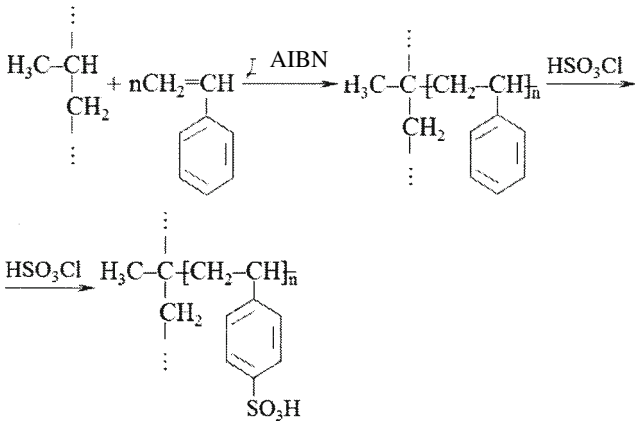
Fig. 2.

Fig. 1. Antimicrobial activity of PCA-GMAA threads containing doxycycline [4.5 (1) and 13.4 (2) %]; gentamicin [5.5 (3), 10.5 (4), 15.0 (5), and 21.2 (6) %]; and kanamycin [7.5 (7), 13.0 (8), and 19.5 (9) %].

Fig. 2. Antimicrobial activity of PP-S threads containing doxycycline [8.6 (1) and 15.5 (2) %]; gentamicin [6.7 (3), 11.2 (4), 16.3 (5), and 28.7 (6) %]; and kanamycin [7.2 (7), 10.2 (8), and 14.4 (9) %].

The following graft-polymerization conditions were recommended for producing carboxylate-containing PCA threads with grafted MAA (called further PCA-GMAA) that had SEC 2.5 mmol/g and strength 18.8 cN/tex: MAA concentration 5.3%; Mohr's salt concentration 2.5%, 70°C, and 60 min reaction time.

PP threads were given highly acidic properties by grafting styrene to them and sulfonating the grafted polystyrene:



The thread was soaked beforehand in 4-5% initiator solution (azobisisobutyronitrile, AIBN), which caused the PP to swell. It was wrung out to 2.5-3.0 and treated for 3-4 h at 80-90°C in an aqueous styrene emulsion. As a result, 13-14% polystyrene was grafted to the thread. The sulfonating agents were 0.3-0.4% sulfuric anhydride in CCl_4 or 0.7-1.1% chlorosulfonic acid in dichloroethane. Treatment at 40°C for 2.5-5.0 h, respectively, provided modified PP-S threads with sulfonate SEC 0.6-0.9 mmol/g.

Anion-exchange PP threads (PP-GMVP) were produced by graft copolymerization of 2-methyl-5-vinylpyridine using a post-irradiation initiation method (SEC 1.75 mmol/g).

Aminoglycoside (gentamicin and kanamycin), tetracycline (doxycycline), lincosamide (clindamycin), and penicillin (ampicillin and carbenicillin) antibiotics were used to impart antimicrobial properties to the modified threads.

Trends in the absorption of antimicrobial drugs by fibrous ion exchangers were examined.

Antimicrobial threads with different durations of activity and efficacies could be created by using fibers and drugs with basic and acidic groups of different ionic strength. A study of the absorption trends on weakly acidic PCA-GMAA, strongly acidic PP-S, and weakly basic PP-GMVP threads found that ion exchange should be performed on

PCA-GMAA and PP-GMVP threads in the salt-form and on PP-C, in the salt- or H^+-form, according to the degree of dissociation of the ionizable groups and the energy changes of water in the ion-exchanger.

Increasing the antibiotic content in the bath was associated with increased absorption but decreased selectivity of them from solution. Absorption by PCA-GMAA and PP-S threads was carried out from solutions of concentration 2.2-3.0 mM; by PP-GMVP threads, 4.0-8.0 mM, in order to produce antimicrobial threads containing ~10% antibiotic according to medical and technical requirements. Kinetic functions obtained at 20 and 40°C showed that absorption equilibrium for all modified threads was practically achieved in 3 h.

Preclinical trials of antimicrobial SSM included the determination of their therapeutic efficacy and duration of action, evaluation of the effect of the threads on the formation of granulated tissue and the proliferative potency of fibroblasts, pathomorphological studies of the healing processes of wounds sutured by them, tests of the threads for carcinogenicity and toxicity, and establishment of the allowed shelf life. Both the initial antimicrobial activity of the threads and that after residing in subcutaneous mouse cells were determined in dense growth medium using the infected agar method against *Bacillus subtilis* test strain (Figs. 1 and 2). The results indicated that the antimicrobial properties of the SSM depended strongly on the type of ionizable groups of the used drugs and modified threads.

Increasing the antibiotic content in the thread at first slightly increased the antimicrobial activity and then gradually reached a plateau. The spectra of antibacterial activity of the diffusing antibiotics corresponded to their usual spectra of activity.

It was found that treated threads with antibiotics suppressed completely the proliferation along them of viable microorganisms. Resection of colons in mongrel dogs and subsequent colon anastomosis using PP threads with gentamicin showed that the antibiotic content in the anastomosis area reached 156 μg/g whereas the antibiotic was not found in the blood and untreated colon sections. An amount of thread containing significantly less antibiotic than for its systemic administration was used to form the anastomosis.

Tests at the N. N. Blokhin Russian Oncological Research Center, RAMS, showed that both the preliminary chemical modification of the threads and the introduction into them of the antibiotics at concentrations giving the SSM high antimicrobial activity did not hinder reparative processes in the sutured wounds.

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