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A New Composite Plate for Hemostasis in Parenchymal Organ Surgery

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Abstract **Introduction.** During trauma of parenchymal organs and closure of wound defects using special coatings, surgeons are faced with the problem of their functional versatility. A variety of collagen sponges and bands used in clinical practice have only a hemostatic effect. **The aim** of the study was experimental substantiation of the efficiency of a new polymer band implant for stopping parenchymal bleeding in surgery. **Material and methods.** The authors have demonstrated the effect of the new hemostatic implant, which was confirmed by laboratory, experimental studies, and morphological evaluation of tissues at the point of contact with the composite plate. **Results.** The results of in vitro studies have shown that the composite hemostatic band shortens the blood clotting time, which indicates an increase in the total coagulation activity of whole blood. This will allow to use it as a local hemostatic agent. **Conclusion.** The developed plate has a very high adhesive ability to a wet surface, the degree of which can ensure the stopping of not only capillary, but also mixed bleeding from parenchymal organs.

Keywords Liver, Bleeding, Hemostasis, Plate, Experiment

1. Introduction

As a result of abdominal injuries or extended surgical interventions, extensive wound defects are often formed, the restoration of which with the use of local tissues is not possible. It leads to the development of a number of complications such as: bleeding, lymphorrhea, prolonged healing, infection, formation of adhesions, etc. Injuries lead to 10% of all deaths worldwide, and blood loss is the most common preventable death cause after injury. Bleeding and hemorrhagic shock are the cause of 30-40% of traumatic deaths [1-5].

The closure of wound defects using special coatings faces the problem of their functional universality. A variety of collagen sponges and bands used in clinical practice have only a hemostatic effect; biological adhesives are designed to connect tissues; anti-adhesive gels are used only to prevent the adhesive process [6-11].

Effective and rapid hemostasis is critically important in surgical operations and emergency injuries. Hemostatic materials currently available include collagen (Col), gelatin (GE), alginate (AG), chitosan (CS), oxidized cellulose, cyanoacrylic acid-based tissue glue and porous zeolite. All of them have an effective hemostasis function, but they also have disadvantages [12-18].

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The efficiency of hemostatic agents based on natural polymers should be based on the fact that they still have a lower potential effect than inorganic hemostatic materials. Advanced products for effective treatment of medical and surgical wounds include hemostatic agents, fibrin and other sealants, high-strength medical adhesives and products preventing postoperative adhesions [19-24].

There is a need to develop unique hemostatic agents that can deliver a hemostatic agent in a few seconds and stop bleeding within two minutes at the site of injury, without any intervention in the form of manual pressure on the wound area or any special preparation for their use. There is also a need to develop more hemostatic agents that can remain functional for a longer time without the need for replacement. Based on this, additional research is needed to analyze performance close to "real world" situations, which often requires unique and personalized injuries and clinical conditions.

The aim of the study was experimental substantiation of the efficiency of a new domestic polymer band implant for stopping parenchymal bleeding in surgery.

2. Material and Methods

We have developed a version of the hemostatic band, which has a complex composition and is a composite material. The main composition of the composite material is cellulose derivatives:

- A layer that provides high adhesion to the wet surface of biological tissues and is a band of Na-CMC (85%) + Ca^{2+} ions at a concentration of 15% with a thickness of 50 microns;
- The second layer is an enhanced hemostatic layer composed of Na-CMC (63%) + oxidized viscose (12%) + Ca^{2+} ions (25%). There are fibers of oxidized viscose in the second layerwith a thread thickness of up to 25 microns and a distance between the fibers of 500-1000 microns;
- The outer layer is a hydrophobic band up to 10 microns thick from vegetable oil (cottonseed oil) (Fig. 1).

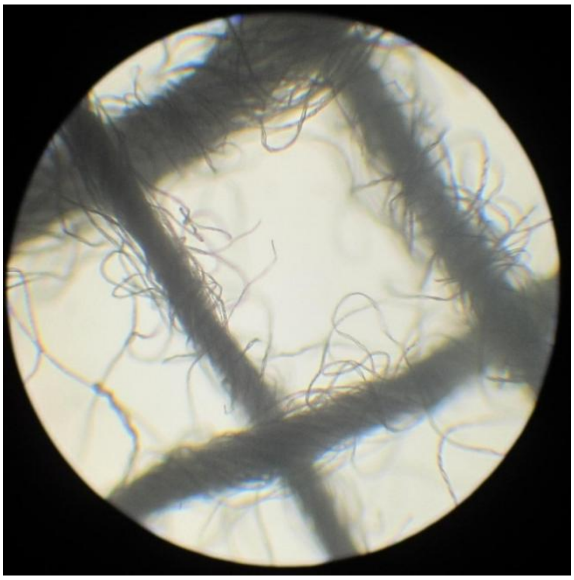

Figure 1. Hemostatic band. The structure of the band of the mesh component from the OC. x40. SM

Viscose fiber is extracted by processing natural plant cellulose and is considered a modification of cellulose fiber called hydrate cellulose (Fig. 2). In our study, the native state of both fibers was evaluated using a stereomicroscope (MSP-2 LOMO).

Figure 2. Viscose fiber. x40. SM

At the same time, viscose, when visually examined, is free of defects, smooth, transparent, the thickness of the fibers is the same. Cotton cellulose fiber consists of many small fibers and is not smooth. The thickness is not the same along the length of the thread and varies unevenly.

Table 1. Breaking strength of the fibers included in the composite coating

Fiber		Cellulose gauze	Viscose
Initial adhesion strength	(Pa)	512	114
30 minutes		498	97
60 minutes		495	85
90 minutes		490	74
2 hours		427	52
3 hours		366	28
4 hours		303	Completely decomposed
5 hours		292	
10 hours		241	
15 hours		194	
20 hours		101	

Table 2. The physico-chemical properties of the composite hemostatic band

№	Physical properties	OC	CMC	Cellulose Mesh	Mesh from OC	CMC+Ca++, Viscose
	Solubility in water(sec)	5.8 + 0.4	600	-	5	600
	Tensile strength(g)	50	150	-	70	200
	Adhesiveness (g)	50	100	20	60	250
	Destruction by heating or sterilization	-	-	-	-	-
	Plasticity (brittleness) (bending in x^o)	120	90	-	70	90
	Durability during storage	Durable	Durable	Durable	Durable	Durable
	Dynamics of strength reduction in water up to 100 mm water column/sec	1	120	-	2	200
	Hygroscopicity in %	50	100	300	300	400

When studying the effect of oxidants (oxidizer - 12% sodium hypochlorite solution) on the breaking strength of the fibers that make up the composite coating, it was found that the breakage of the viscose fiber increases over time, and the effort spent on breaking decreases compared to cellulose fiber (Tab. 1).

Both fibers were changed in different ways under the influence of oxidants. Cotton cellulose showed high resistance, the degree of fiber breakage decreased only by 1.5 times in 4 hours. Viscose fiber lost strength 3 times in 3 hours, completely disintegrated by 4 hours.

The adhesion of the fibers was also evaluated. As a result of the tests, it was found that the adhesive ability of the viscose composite material is equal to 961 pascal (Pa).

Visual and stereomicroscopic evaluation of the new composite coating shows that the fibers were distributed in the center of the composite band and form a single unit with other components of the band. When examined under a stereomicroscope, the gauze fibers completely retained their mesh structure. The band thickness was 2 mm.

The physico-chemical properties of the composite hemostatic band in comparison with the control samples are shown in Table 2.

3. Results

Adhesion of composite material. Taking into account the properties of the composite band, we have developed a device for studying the adhesion to various materials and fabrics.

The results obtained were calculated using the following formula: adhesive strength (F): F= mg. Here m - weight, g - acceleration of gravity 9.8 m²/c. Then the stickiness was calculated: F/S. Ra (Pascal) was chosen as the unit of measurement. The test substance, cut into 1 cm * 1 cm on the surface of the device, was evenly mixed with 100 µl of water. Lifting threads were attached to the attached cover glass with a small groove. We waited one minute, then attached it to the clamp, conducted an experiment to change the weight and studied it by adding water to the wetted part of the equipment. In this case, the density of water was assumed to be 1 g/cm^3.

Table 3-7 shows the results on the chemical properties of the implant, In vitro, In vivo – morphological, In vivo – biochemical and toxicological studies.

Table 3. Chemical properties of composite hemostatic band

№	Chemical properties	1	2	3	4	5
1.	pH in solution	5	5	2	3	5
2.	pH in plasma	5	5	3	4	6
3.	Chemical reaction in tissues	-	-	-	-	-
4.	Decomposition products in tissues	CO_2 and H_2O	CO_2 and H_2O	Hydrolysis + phagocytosis	CO_2 and H_2O Hydrolysis + phagocytosis	CO2 and H_2O Hydrolysis + phagocytosis
5.	Interaction with antiseptics and medicines	-	-	-	-	
6.	Resistance to chemical sterilization	+	+	+	+	+
7.	Destruction when heated or sterilized	-	-	-	-	-

Note: 1 - OC; 2 - CMC; 3 - Cellulose Mesh; 4 – Mesh from OC; 5 - CMC+Ca++, Viscose

Table 4. Results of in vitro studies

№	in vitro studies	1	2	3	4	5
1.	Solubility in biological fluids (sec)	5	15	-	5	20
2.	Clotting time in a drop of blood	7	2	2	3	1
3.	Formation of fibrin in plasma	-	1	x	x	2
4.	Coagulogram in interaction with blood	-	1	2	3	1
5.	Clotting time with banked blood	-	3	4	5	2
6.	Adhesion to the surface of the isolated liver	50	150	20	80	250
7.	Adhesiveness in the presence of blood and plasma to liver tissue	+	100	10	-	200
8.	Time of loss of form during interaction with liver tissue (sec)	5	10	-	5	12
9.	Bactericidal activity	-	-	+	-	+++

Note: 1 - OC; 2 - CMC; 3 - Cellulose Mesh; 4 – Mesh from OC; 5 - CMC+Ca++, Viscose

Table 5. Results of In vivo studies - morphological

№	Parameter	1	2	3	4	5
1.	Evaluation of hemostatic effect on rat liver wound model visually during surgery	-	2	3	4	2
2.	Adhesiveness evaluation	+	+++	+	+	+++
3.	Examination of the band condition immediately after implantation	-	+++	++	+	+++
4.	Features of sticking with surrounding fabrics and tools	++	+++	+	++	+++
5.	Working properties on a bleeding surface	+++	++	+	+	+++
6.	Visual evaluation of the liver condition during the observation period	+++	+	+	+	+++
7.	Evaluation of the presence and severity of adhesions	-	++	++	+++	+

Note: 1 - OC; 2 - CMC; 3 - Cellulose Mesh; 4 – Mesh from OC; 5 - CMC+Ca++, Viscose

Table 6. Results of In vivo studies - biochemical

№	Parameter	1	2	3	4	5
1.	Blood clotting time studies			+		+
2.	Blood coagulation studies			+		+
3.	General blood tests studies			+		+
4.	Biochemical blood tests studies			+		+

Note: 1 - OC; 2 - CMC; 3 - Cellulose Mesh; 4 – Mesh from OC; 5 - CMC+Ca++, Viscose

Table 7. Results of toxicological studies

Toxicity	1	2	3	4	5
Acute			+		+
Chronic			+		+

Note: 1 - OC; 2 - CMC; 3 - Cellulose Mesh; 4 – Mesh from OC; 5 - CMC+Ca++, Viscose

4. Discussion

Ex vivo studies. Isolated sheep liver with a shelf life of no more than 1 hour in saline solution was used to evaluate adhesion to biological tissues. 1 cm^2 of a hemostatic band was attached to the liver surface and the adhesion strength was measured using the technique described above (Fig. 3).

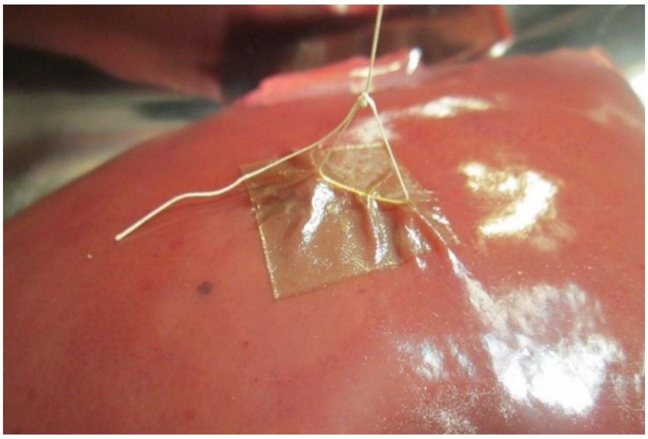

Figure 3. The beginning of the band shrinkage with increasing load

As a result of the tests, it was found that the adhesiveness of the prepared composite material using oxidized viscose was equal to 961 Ra (Pascal), which was a sufficient indicator for covering the wound surface, tight fixation and non-separation from it. In general, in a comparative aspect, among the various variants of cellulose-based biomaterials, it was found that the inclusion of oxidized viscose in the composition improved the physico-chemical properties of the composite hemostatic band, including the best indicators of tensile strength, adhesion to the surface of the isolated liver, as well as in the presence of blood and plasma, hygroscopicity and bactericidal activity.

A composite hemostatic band reinforced with viscose fibers was used as a material for experimental studies. The control was a plate reinforced with cotton cellulose fibers.

The study of blood clotting time according to the Lee-White method. A composite hemostatic band in the amount of 1 cm^2 was added to a test tube with 1 ml of venous blood. A test tube with blood was placed on a water bath at 37℃, and a stopwatch was detected at the same time. 2 minutes after placing the blood, and then every 30 seconds, the tube was gently tilted at an angle of 60-45°. Blood flowed freely along the tube wall at the beginning of the study. The determination was carried out until a dense clot was formed. The time of blood clotting was considered to be the time from the moment of immersion of the hemostatic band into the test tube to the appearance of a clot, which made up 5.27 ± 0.50 seconds. Donation whole blood served as the study control. According to this study, the time of blood clotting in the control group was 11.2±0.54 sec. Normally, according to this method of investigation, the blood clotting time ranges from 4 min 55sec to 11 min 44sec.

The results of in vitro studies have shown that the composite hemostatic band shortens the blood clotting time, which indicates an increase in the total coagulation activity of whole blood.

5. Conclusions

In a comparative aspect, among the various variants of cellulose-based biomaterials, it was found that the inclusion of oxidized viscose in the composition provided an improvement in the physico-chemical properties of the composite hemostatic band, including the best indicators for tensile strength, adhesion to the surface of the isolated liver, as well as in the presence of blood and plasma, hygroscopicity and bactericidal activity.

Thus, the developed plate has a very high adhesive ability to a wet surface, the degree of which can ensure the stopping of not only capillary, but also mixed bleeding from parenchymal organs.

The possibility of having a hemostatic property was justified by the results of in vitro studies, which showed that the composite hemostatic band shortens the clotting time of blood, which, therefore, indicates an increase in the total coagulation activity of whole blood. This will allow it to be used as a local hemostatic agent.

The authors declare no conflict of interest.

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The article is published for the first time and is part of a scientific work.

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