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Assessment of the Efficiency and Biocompatibility of Filters for Hyperbaric Plasma Sorption

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Abstract

The authors analyze 50 patients treated for 2018-2019 in the clinic of the Andijan state medical institute with severe course of MJ against the background of gallstone disease, complicated by choledoholitis. All patients are divided into two groups. The main group includes 19 patients treated for 2019. In the comprehensive treatment of these patients after endoscopic or surgical elimination of the cause of MJ (choledocholyitis) an advanced method of hyperbaric plasmasorption is applied. The comparison group includes 31 patients treated for 2018, whose rehabilitation applied the standard protocol of management of patients with complicated course of MJ.

The authors conclude that polymer substrates of cotton cellulose at long incubation reliably accelerate the clotting of donor plasma and have the ability to absorb fibrinogen, affecting the state of hemostasis.

The urgency of the problem. In the complex therapy of liver failure in patients with obstructive jaundice (MJ), such methods of extracorporeal hemocorrection as plasmapheresis and plasmasorption are most often used, the effectiveness of which is limited by the volume of removed blood components. MARS and Prometheus systems (separation and adsorption of fractionated plasma) are not widely used due to the high cost of consumables. In this connection, at present, a promising direction in extracorporeal detoxification (ECD) is the use of sorption methods with a certain selectivity [2, 9, 11, 15].

Extracorporeal filtration sorbent technologies combine the first stage of plasma separation and adsorption of cytokines, inflammatory mediators and / or toxins, exclude the interaction of the cellular composition of blood with a foreign surface of a carbon or other type of sorbent [1, 5, 10]. In view of the lower complication rate compared to hemoperfusion, plasma perfusion is a safer and more suitable method for purifying large plasma volumes (6-15 liters per procedure) [3, 7, 8, 12, 13].

However, modern organ transfusion replacement and organ protection are deeply rooted in tradition. Lack of scientific support and advice often leads to conflicting opinions. Therefore, the development of new technologies for organ protection and rational therapeutic algorithms supported by scientific data is very useful [4, 6, 14].

The questions of choice, timing of pazma exchange and plasma sorption procedures, selection of patients who potentially have the opportunity to obtain the greatest benefit from this type of ECD, ways of preventing the loss of nutrients and evaluating the effectiveness of therapy in liver failure in the presence of breast cancer remain open.

The aim of the study is to improve the results of surgical treatment of patients with endogenous intoxication and hepatocellular insufficiency against the background of obstructive jaundice by developing an original method of extracorporeal detoxification.

Materials and research methods. The subject of the study was 50 patients treated in 2018-2019 in the clinic of the Andijan State Medical Institute with a severe course of breast cancer on the background of cholelithiasis complicated by choledocholithiasis. All patients

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are divided into two groups. The main group included 19 patients treated in 2019. In the complex treatment of these patients after endoscopic or surgical elimination of the cause of breast cancer (choledocholithiasis), an improved method of hyperbaric plasma sorption was used. The comparison group included 31 patients who were treated in 2018, in whose rehabilitation a standard protocol was applied for the management of patients with a complicated course of breast cancer, 38 women (74%), 12 men (26%).

Four types of polymers were studied as a potential polymer substrate for the filter of the EPC system: borosilicate glass, polypropylene, cotton cellulose, and modified cellulose. At the same time, the filter must be able to withstand increased pressure during hyperbaric plasma sorption and effectively retain coal microparticles larger than 2 microns.

a) Borosilicate glass filters.

The borosilicate glass from which the filters were made had the following composition (Table 1).

Table 1

Composition of borosilicate glass polymer substrate

Component	Content, weight. % based on oxide	Component	Content, weight. % based on oxide
SiO_2	73	CaO	0-2
B_2O_3	8-10	BaO	2-4
Al_2O_3	4-5,6	ZrO_2	0-2
Li_2O_3	0,5	CeO_2	0-1
Na_2O	7-9	F	0-0,5
K_2O	1,2-2,5	MgO	0,1

Glass filters were polished plates of crushed and then sintered glass with an average pore diameter of 3-40 μm, which corresponds to the classes according to GOST 9775-69 (Table 2).

Table 2

Glass filter classes

Filter No.	Class according to GOST 9775-69	Average pore size, μm	Plate thickness, mm	Permeability for H2O, ml / (cm2s * Pa)
1	160	100-160	3,3	2*10-4
3	40	16-40	2,8	2*10-4
4	10	10-16	2,3	3*10-5
5	3	3-6	2,2	2*10-6
6	2	1-2	2,0	2*10-6

We used the following borosilicate glass filters (Fig. 1).

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Figure: 1. Appearance of borosilicate glass filters.

b) polymer substrates for polypropylene filters had the form of membranes with an average pore diameter of 5-100 μm, chemical resistance at a pH range of 3-14. Polypropylene fabrics are sufficiently resistant to the action of acids, bases and strong oxidants, and in terms of mechanical strength they are close to mylar fabrics; they dissolve in gasoline, xylene and tetrachloroethane, and above 110 ° C they quickly lose their strength.
A general view of a polypropylene membrane filter and its ultrastructure are shown in Fig. 2.

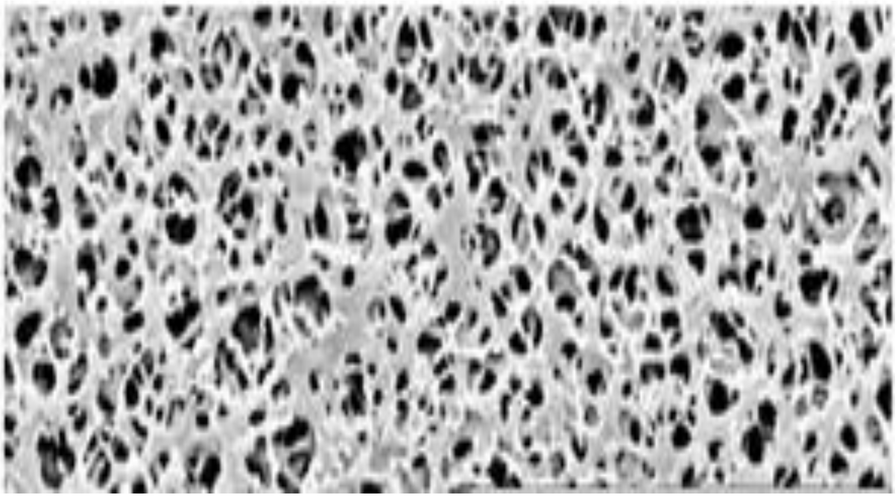


Figure: 2. Membrane filter made of polypropylene (light microscopy, 10x4).

c) samples of polymer substrates for cotton cellulose filters were provided by the Institute of Polymer Chemistry and Physics. A general view of a membrane filter made of cotton cellulose is shown in Fig. 3.

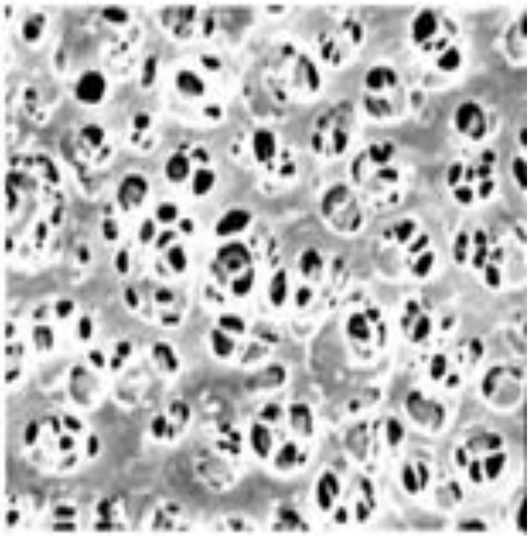
b.  b. 

Figure: 3. Microstructure of a cotton cellulose filter: a) - light microscopy, 10x1; b) light microscopy, 10x41

In the choice of polymer substrates for filters for the ED system, we were guided by the fact that blood plasma will be used as the biological fluid to be purified, i.e., as is customary in analytics, the composition of the suspension, the type of solvent and the temperature of the separated phases were taken into account.

Research results and their discussion. The list of physical and chemical properties of cotton cellulose according to GOST 505-79 is presented in table No. 3, we used grade 150 cellulose with the lowest viscosity and low mass fraction of water.

Table 3
Physicochemical properties of cellulose in accordance with GOST 505-79

Indicators	1st grade	mark 150	mark 250	mark 350	mark 650
Mass fraction of alpha-cellulose,%, not less	98,0	99,1	99,2	99,2	99,2
Wettability, g, not less	140	120	120	110	110
Mass fraction of water,%, no more	10,0	8,0	8,0	9,0	9,0
Mass fraction of ash,%, no more	0,2	0,13	0,10	0,14	0,12
Mass fraction of residue insoluble in sulfuric acid,%, no more	0,30	0,20	0,15	0,17	0,15
Mass fraction of fibrous dust,%, no more	2,0	–			–
Whiteness,%, not less	85	85	83	85	86
Dynamic viscosity, mPa.s	116-175	172	220	312	635

So, in the sample of cotton cellulose we used, the solubility in water is 10 mg / l at 20 ° C, the melting point is -2200 ° C, the wettability is 120 g, the mass fraction of water is 8%, the mass fraction of ash is 0.13%, the mass fraction of the residue is insoluble. in sulfuric acid - 0.2%. Microscopy of a polymer substrate made of HC revealed that the nature of the pores is irregular,

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they are large, of different sizes, and randomly located (Fig. 4).

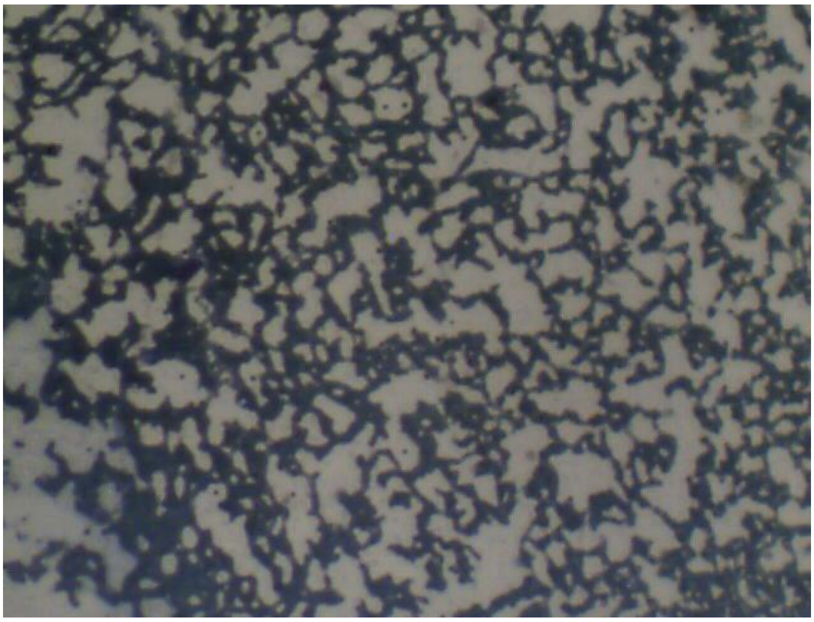

Figure: 4. Microstructure of a polymer substrate in the form of a HC filter. Magnification 10 * 4 (40 times), stereomicroscopy (3D). A large-pore structure is visible, the pores are of different sizes, randomly located.

Characteristics of borosilicate glass polymer substrate for EPC filter.A borosilicate glass filter with a pore diameter was studied: filter S4-P16 with a pore diameter of 1-2 microns (No. 6 according to GOST 9775-69) with a water permeability of 3 * 10-5 ml / (cm2s * Pa). Borosilicate glass is chemically and biologically inert and resistant to almost all known substances. Due to its high resistance to aqueous solutions of salts, organic substances, halogens (chlorine, bromine) and to most acids, it can be used in cases where other materials cannot be used, in addition, it is heat-resistant (operating temperature up to 500 degrees Celsius), heat-resistant and due to the above properties - biologically inert.

Due to its high hydrolytic stability, this glass is especially suitable for pharmaceutical applications. The chemical resistance of borosilicate glass is determined by its hydrolytic resistance, which is determined according to DIN ISO 719 and complies with the standard. The maximum value for chemically highly resistant glass belonging to hydrolytic class 1 is 31 μg Na 2 O / g. The acid resistance S is determined according to DIN 12116. The maximum loss for glass belonging to acid class 2 is 1.5 mg / dm2. Alkali resistance L is determined according to DIN ISO 695. The maximum loss for glass belonging to alkaline class 2 is 175 mg / dm2. Thus, borosilicate glass is hydrolytically stable and bioinert.

Features of the polypropylene polymer substrate for the EPC filter. The polypropylene backing is a filter for the Diacap Polysulfone system manufactured by B. Braun, Germany. The chemical composition of polypropylene is as follows: [- CH2-CH (CH3) -] n.

Physicochemical properties of polypropylene: high resistance to the effects of the body's environments, does not change its initial characteristics with repeated deformations, allows for thermal, radiation and chemical sterilizing treatment. Parts of artificial heart valves are made of polypropylene, which proves its bioinertness.

A polypropylene filter for the Diacap Polysulfone system produced by B. Braun, Germany

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completely retains the particles of the carbon sorbent, which is confirmed by the permission of the Pharm Committee of the Republic of Uzbekistan for use.

Comparative analysis of polymer substrates for filters for EKD by the property of retaining sorbent particles (coal). The study of the optical density of the filtrate of the suspension of the carbon sorbent, as well as counting the number of coal particles in the Goryaev chamber after passing through filters made of various polymer substrates (filters made of polypropylene, borosilicate glass with different pore diameters, filters made of cotton and modified cellulose with an unknown pore diameter) showed that the most optimal is a filter with a pore diameter of 10-16 microns, perhaps the pore diameter in the modified cellulose filter corresponds to that of the S4-P16 filter (Table 4).

Table4
Results of a comparative analysis of the ability to retain particles of a carbon sorbent of polymer substrates

Name of the polymer backing	Pore diameter	Optical density of the filtrate (E) at a wavelength of 540 nm in a 1.0 mm cuvette	Counting coal particles in the Goryaev chamber, 1012 / l
Control	-	0,900 ± 0,018	Quite more 30,0 x 10^{12}/ л
S6-P16	1-2μm	0,0182 ± 0,0011	0,11 ± 0,05
t-test to control	-	t-48,90; p<0,05	p<0,05
Polypropylene	unknown	0,011 ± 0,006	0,276 ± 0,004
t-test to control	-	t-46,85; p<0,05	p<0,05
Cotton pulp	unknown	0,380 ± 0,049	15,362 ±2,576
t-test to control	-	t-9,96; p<0,05	p<0,05

Discussing the results obtained, we note that the pore diameter of the cotton cellulose filters is rather large, as a result of which the transmission of particles of the carbon sorbent occurred, which led to a high optical density of the filtrate, while the pore diameter of the borite glass filter was much smaller, which caused the retention of particles. coal sorbent and an insignificant optical density of the filtrate, as well as lower counting rates in the Goryaev chamber. The particles of activated carbon have an average size of 30-100 microns.

The use of borosilicate glass was characterized by virtually identical optical density with polypropylene (0.0182 ± 0.0011 E and 0.011 ± 0.006 E), but a higher filtration capacity was determined in relation to the retention of particles of the carbon sorbent (0.11 ± 0.05 versus 0.276 ± 0.004 x 1012 / L; p <0.05) (Table 4; Fig. 5).

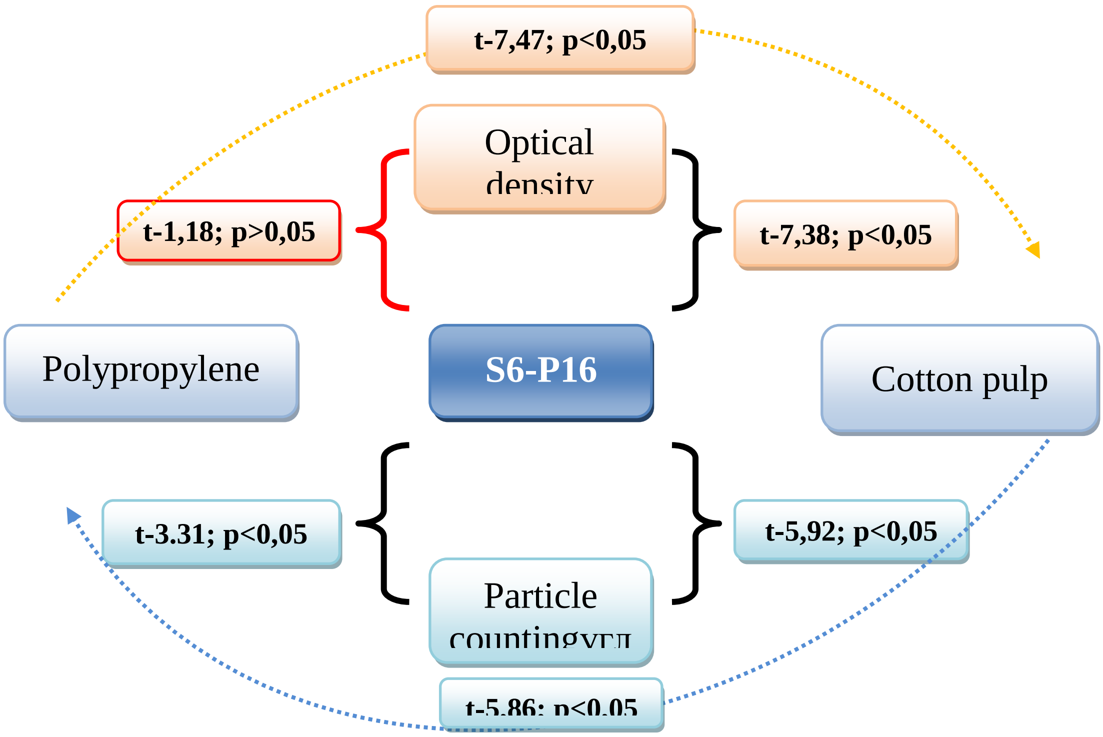

Figure: 5. Reliability of the ratio of optical density and the number of carbon particles when using various filters (the best values are determined for borosilicate glass).

A comparative analysis of the data of light microscopy, optical density and counting in the Goryaev chamber of the filtrates obtained using inert filters made of borosilicate glass of various diameters showed that the polymer substrate made of cotton cellulose showed the worst results in terms of the properties of retaining sorbent particles, comparable to those of the S6-P16 filter. with a pore diameter of 1-2 microns.

Conclusion. Thus, during prolonged incubation, polymer substrates made of cotton cellulose significantly accelerate the clotting of donor plasma and have the property of adsorbing fibrinogen, affecting the state of hemostasis.

Cellulose and polypropylene are promising raw materials for the development of sorbents and filters for extracorporeal detoxification systems, which are cost-effective and readily available in our country. However, these categories of filters are not able to prevent the passage of coal microparticles during hyperbaric flame sorption. These requirements are fully met by glass borite filters with specified pore parameters. Glass filters have a distinct advantage in terms of biocompatibility and the ability to withstand any sterilization option. Borite filters can withstand extreme pressure figures to ensure reliable prevention of the passage of microparticles of carbon sorbents.

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