ISSN: 0975-833X

*Available online at http://www.journalcra.com*

*International Journal of Current Research*
*Vol. 11, Issue, 10, pp.7771-7773, October, 2019*

**DOI: https://doi.org/10.24941/ijcr.36605.10.2019**

**INTERNATIONAL JOURNAL OF CURRENT RESEARCH**

## REVIEW ARTICLE

# TO EXPERIENCE IN THE EXPERIMENT THE HEMOSTATIC AND AEROSTATIC PROPERTIES OF HEPROCEL IN THE FORM OF FILMS FROM CARBOXYMETHYL CELLULOSE DERIVATIVES

**Sadykov, R.A., Ismailov, B.A. and *Marufkhonov, O.N.**

Department of the experimental research laboratory, Republican Specialized Scientific, Center of Surgery named after Vakhidov V.V. Tashkent. Uzbekistan

**ARTICLE INFO**

*Article History:*
Received 14th July, 2019
Received in revised form
18th August, 2019
Accepted 05th September, 2019
Published online 30th October, 2019

*Key Words:*
Oxidized Cellulose, Hemostasis, Aerostasis, Surgery, Bleeding.

**ABSTRACT**

The study determined the hemostatic activity of import-substituting hemostatic material of local action, obtained as a result of oxidation of unregenerated cellulose, in models of laboratory animals (outbred dogs).It was established that the studied sample of oxidized cellulose has hemostatic and aerostatic activity, which in its indicators is comparable to that for the well-known material "Heprocel":its use after applying a model of cut wound to the right lungs of dogs led to a decrease in the intensity of blood loss by 25% of the severity of spontaneously stopping bleeding, and the time to stop bleeding was 330 ± 35 s



***Citation: Sadykov, R.A., Ismailov, B.A. and Marufkhonov, O.N.*** **2019.** "To experience in the experiment the hemostatic and aerostatic properties of Geprocel in the form of films from carboxymethyl cellulose derivatives", *International Journal of Current Research*, 11, (10), 7771-7773.

## INTRODUCTION

Bleeding that occurs in the intra- and postoperative periods is one of the most important problems of modern medicine (Orlov *et al*., 2014). According to world literature, postoperative bleeding increases hospitalization by an average of 3.3 days, and the cost of treatment - by 19.9% ( Ye *et al*., 2013). Forced blood transfusion is associated with an increased risk of viral and bacterial infection. For example, in France, a blood-borne bacterial infection occurs in 2.4 cases per 1 million units of transfused red blood cells, in 24.7 cases per 1 million units of transfused platelet concentrate and in 0.4 cases per 1 million units of transfused fresh frozen plasma, and severe forms of this infection - with a frequency of 13.4 cases and 5.1 deaths per 1 million units of transfused thrombocyte concentrate (Lafeuillade, 2000). All of the above significantly worsens the course of the postoperative period and increases the duration of hospitalization. There is a wide variety of traditional methods of stopping bleeding (mechanical, chemical, thermal, etc.),but special attention is paid to local hemostatic agents that have an effective local effect and can be used in cases of diffuse bleeding (wound surface of the parenchymal organ, spongy tissue, etc.).

***Corresponding author:*** **Marufkhonov, O.N.,**
Department of the experimental research laboratory, Republican Specialized Scientific, Center of Surgery named after Vakhidov V.V. Tashkent. Uzbekistan.

In a comparative assessment and selection of hemostatic drugs, their safety, effectiveness, ease of use, cost, availability and other factors are considered (Spotnitz, 2008). Despite the presence of a large number of drugs, there are no universal hemostatic agents. Therefore, the development of tools and methods to combat bleeding remains one of the main tasks of surgery. Today, one of the priority areas of research and development in medicine is the creation of new biocompatible and biodegradable products for surgery. In this regard, hemostatic preparations based on oxidized cellulose (OC) are of great interest, which, due to its structure and plant origin, has such important properties as biocompatibility, biodegradability, nontoxicity, chemical inertness, fibrousness, mechanical strength, and insolubility in water. The most famous and widely used in medicine hemo-static material based on oxidized cellulose is the drug "Heprocel". The hemostatic drug Heprocel is used in various fields of surgery, in particular in abdominal surgery.So, its intraoperative use after resection of the liver and with diffuse bleeding of soft tissues allows to reduce the volume of drainage losses in the postoperative period by 1.5-1.8 times (Belov, 2009; Tavlasoglu *et al*., 2013; Wang *et al*., 2011). The use of OC-based materials in hepatobiliary surgery is described in a prospective, randomized, multicenter, blind study, where a comparison of the efficacy of Veriset hemostatic agents (oxidized cellulose) and TachoSil (collagen plates with fibrinogen and thrombin) showed that the time for hemostasis when using them was

respectively 1 and 3 minutes. The authors concluded that the use of Verisetcan reduce the volume of blood transfusions, reduce the risks of infection and the occurrence of postoperative complications, as well as the length of hospital stay (Ollinger, 2013). Examples of the effective use of hemostatic materials based on oxidized cellulose in various fields of surgery are presented in the review (Chernyavsky, 2014). Given the absence of Uzbek analogues of hemostatic agents based on OC, as well as its great innovative potential, which consists in its ability to further functionalize with the release of complex-acting drugs, the creation of domestic hemostatic material of local action based on OC is an urgent and promising task.

**The purpose of the work:** An experimental study of a domestic hemostatic agent based on OC.

## MATERIALS AND METHODS

The experiments on the study of the hemostatic and aerostatic properties of the preparation “Heprocel” and the studied hemostatic film (OC sample) were conducted on 8 outbred dogs weighing 7500-9000 g.Care for experimental animals and their maintenance in vivarium conditions were standard and met the requirements of the orders “Sanitary Rules for the Design, Equipment and Maintenance of Vivariums” No. 267 dated 06/19/2003 of the Ministry of Health of the Russian Federation, “Rules for the Treatment, Maintenance, Anesthesia and Killing of Experimental Animals” of the Ministry of Health SovetUninon (1977), the principles of the European Convention (Strasbourg, 1986) and the Helsinki Declaration of the World Medical Association on the Humane Treatment of Animals (1996).

The criteria for the manifestation of hemostatic properties in the studied drugs were considered to be a decrease in the intensity of blood loss (mg) and a decrease in the time for stopping bleeding (s) in comparison with indicators of spontaneously stopping bleeding (control) and as well as aerostatic ability by preserving lung tissue heretic’s .The stopping time of bleeding was determined by stopping the bleeding after the next removal of a sample of local hemostatic from the wound surface, the amount of blood loss by weighing the matrix before and after soaking it with blood, taking into account the individual characteristics of spontaneously stopping bleeding without hemostatic, the severity of which was described mathematically by the formula of the exponential dependence of its intensity from time to time, and the intensity of the bleeding stopped by the drug.To conclude that the hemostatic activity of one hemostatic is superior to another, extrapolation of bleeding intensity indicators was performed.

## RESULTS AND ITS DISCUSSION

As a result of a series of experiments carried out in assessing the absorbency of hemostatic materials by application to the wound surface, the lungs were found to have both tested materials with good adhesive ability and high hygroscopicity (see figure). When assessing the intensity of bleeding using the above-described method, it was noted that both hemostatic materials significantly reduce the amount of blood loss in comparison with the amount of bleeding that stops spontaneously. Thus, the intensity of bleeding when using a sample of OTs was 0.09 ± 0.01 mg, and when using Heprocel - 0.04 ± 0.01 mg (respectively, 60 and 64% less than the intensity of spontaneously stopping bleeding).

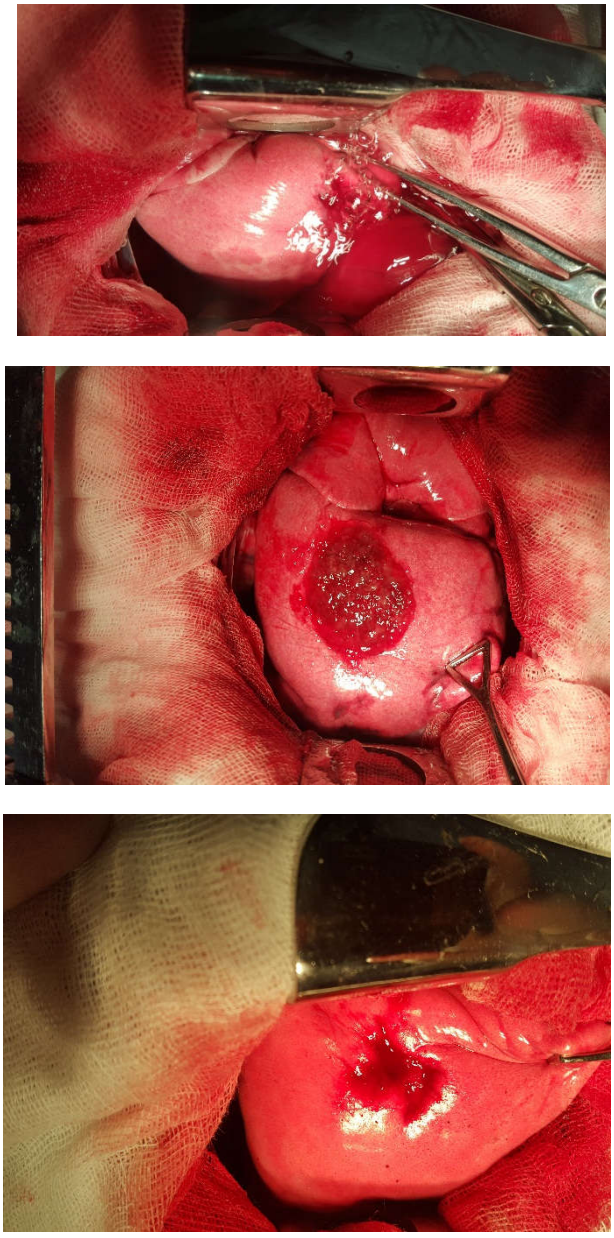

**Fig. Formation of the Geprpocel films (b) and the OC sample (a) to a cut wound in a lung of a laboratory animal**

It was also noted that the time for stopping bleeding when using an OC sample as a hemostatic material is comparable with the data for the Heprocel preparation (330 ± 35 respectively). A study of the mechanism of action of hemostatic materials based on OC was considered in (Cheng *et al*., 2013; Krizova, 2007). Due to its high absorbency, OC absorbs most of the liquid component of blood, thereby increasing its viscosity. Then, due to the negative electric charge of the carboxyl groups that are part of the OC molecule, adhesion and activation of platelets occurs, in addition, due to the low pH value, the OC causes vasoconstriction in the area of its application. It was also noted that the carboxyl groups of OC form complexes with iron ions of blood hemoglobin, which leads to nonspecific platelet aggregation and the formation of an artificial clot (Bajerova *et al*., 2009). During the experiment we also examined aerostatic ability of the Heprocel. During the experiment, an artificial wound was created in the lung tissue. Subsequently, 600 ml of isotonic

solution was injected into the dog's chest, resulting in impaired lung tissue hermetics. The picture shows bubbles come out before using Heprocel. Then the fluid was absorbed. When isotonic fluid was injected into the chest again after using Heprocel, bubbles did not form. The world literature contains a large number of studies aimed at identifying, confirming and comparing various hemostatic materials based on oxidized cellulose, collagen, gelatin, thrombin, etc. in the experiment. So, M. Chalupova *et al*. We studied the hemostatic activity of Gelitacel (hemostatic material based on OC) in comparison with Gelaspon (hemostatic material based on gelatin) in an experiment on Wistar rats. When performing a caudal pole resection with the left kidneys and applications of the studied hemostatic agents to the wound surface, the time for stopping bleeding when using Gelitacel was 1.40 ± 0.18 min, when using Gelaspon -2.33 ± 0.27 min ($p < 0.01$), which says pronounced hemostatic activity of materials based on OC (Chalupova, 2012). In turn, according to I. Takacs *et al*., When comparing materials based on OC (Heprocel) with materials based on bovine collagen ("Sangustop") and horse collagen coated with fibrin and thrombin ("TachoSil"), by performing standard 5-centimeter resection of the liver in an experiment on pigs found that the bleeding time using Sangustop was 140 ± 88 s,"TachoSil" - 243 ± 140 s ($p = 0.005$), Heprocel - 352 ± 70 s ($p < 0.001$), which indicates pronounced hemostatic properties of collagen-based preparations in comparison with OC-based preparations (Takacs, 2010).

In addition to bleeding from a simulated wound of the parenchymal organ of laboratory animals, a model of bleeding from an arterial anastomosis is used as a surgical model for assessing the hemostatic properties of Geprocel in world experimental practice. So, S. Bijan *et al*. compared the hemostatic activity of the absorbable gelatin sponge "Gelfoam", microfibrillar collagen of cattle "Avitene", oxidized regenerated cellulose Heprocel and the hemostatic agent "FloSeal", which contains the gelatin matrix and cattle thrombin, in rabbits, by crossing in the abdominal region and performing an end-to-end anastomosis. The studied hemostatic agent was applied to the seam line of the anastomosis, powder was placed on top of it, and blood flow was started. The intensity of bleeding was determined by weighing surgical gauze. As a result of the experiment, it was found that in terms of hemostatic properties, Heprocel (bleeding intensity 66.7 ± 16.7 ml) is comparable to Gelfoam (66.4 ± 17.6 ml), superior to Avitene (80.6 ± 34.0 ml) and inferior to Flo Seal (44.2 ± 8.5 ml) (Kheirabadi, 2002). Thus, despite the large number of studies aimed at studying the hemostatic and aerostatic activity of hemostatic materials of local action, there is no consensus on the effectiveness of this or that drug, which allows us to conclude that the problem of developing hemostatic drugs of local action is urgent.

**Conclusion**

Based on the foregoing, we can conclude that the OZ sample we obtained has pronounced hemostatic and aerostatic activity, significantly reducing the amount of blood loss and preserving lung tissue hetmetic's when modeling a wound of a parenchymatous organ. The hemostatic activity of the studied sample of OTs is comparable in its indicators with that for the Heprocel material. This OC sample can be used for further studies, in particular, for evaluating resorption properties.

## REFERENCES


Bajerova M., Krejcova K., Rabiskova M. *et al*., 2009. Oxycellulose: Significant characteristics in relation to its pharmaceutical and medical applications // Adv. Polym. Tech. 28. (3). 199-208.

BelovYu, V., Bazylev V.V., Alekseev I.A. 2009. The use of oxidized regenerated cellulose (Surgicel Nu-Knit) in addition to the main methods of surgical hemostasis in cardiac surgery operations // Surgery. (5). 1014.

Chalupova M. 2012. Local tissue reaction after the application of topical hemostatic agents in a rat partial nephrectomy model // J. Biomed. Mater. Res. Pt. A.100. (6). 1582-1590.

Cheng W., He J., Wu Y. *et al*., 2013. Preparation and characterization of oxidized regenerated cellulose film for hemostasis and the effect of blood on its surface // Cellulose.20. (5). 2547-2558.

Chernyavsky A.M., Grigoriev I.A., Morozov S.V. *et al*., 2014. Control of local hemostasis using oxidized cellulose preparations // Surgery. (8). 71-75.

Kheirabadi B.S. 2002. Comparative study of the efficacy of the common topical hemostatic agents with fibrin sealant in a rabbit aortic anastomosis model // *J. Surg. Res.,*106. (1). 99-107.

Krizova P., Masova L., Suttnar J. *et al*., 2007. The influence of intrinsic coagulation pathway on blood platelets activation by oxidized cellulose // J. Biomed. Mater. Res. A. 82. (2). 274-280.

Lafeuillade B., Eb F., Ounnoughene N. *et al*., 2008. Residual risk and retrospective analysis of transfusion-transmitted bacterial infection reported by the French National Hemovigilance Network from 2000.

Ollinger R., Mihaljevic A. L., Schuhmacher C. *et al*., 2013. A multicentre, randomized clinical trial comparing the Veriset ™ haemostatic patch with fibrin sealant for the management of bleeding during hepatic surgery // HPB.15. (7). 548-558.

Orlov D., Selby R., Yip P. *et al*., 2014. Platelet dysfunction, assessed during surgery, as an independent predictor of high blood loss in cardiac surgery // Circulatory pathology and cardiac surgery. (3). 97.

Spotnitz W. D., Burks S. 2008. Hemostats, Sealants, and adhesives: components of the surgical toolbox // Transfusion. 48. (7). 1502-1516.

Takacs I. 2010. Efficacy of different hemostatic devices for severe liver bleeding: a randomized controlled animal study // Surg. Innovation.17 (4). 346-352.

Tavlasoglu M., Durukan A.B., Kurkluoglu M. *et al*., 2013. Comparison of sternal intramedullary bleeding prevention strategies in cardiac surgery // *Turk. J. Med. Sci*., 43.695-699.

Wang C., Gu T.X., Yu L. *et al*., 2011. Role of oxidized regenerated cellulose in the hemostasis of severe sternal osteoporosis during cardiopulmonary bypass // *J. lin. Rehabil. Tissue Eng. Res.,*15. (25). 47394742.

Ye X., Lafuma A., Torreton E., Arnaud A. 2013. Incidence and costs of bleeding-related complications in French hospitals following surgery for various diagnoses // BMC Health Serv. Res., 13. (1). 186.