Original Article

Development of an Innovative Surgical Suture Material That Prevents the Formation of Arterial Thrombosis

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Abstract

One of the most serious complications after surgical interventions on the arteries of the lower extremities is thrombosis of the vascular prosthesis. Unfortunately, it is almost impossible to protect the patient from contact with the surgical thread with flowing blood, which makes the location of the surgical operation a focus of thrombosis. The purpose of this scientific study is to evaluate the possibility of modifying the surface of a polypropylene thread with heparin using chemical inoculation in order to increase the thromboresistant properties of the suture material. To do this, a polyhydroxybutyrate/oxivalerate copolymer and a heparin solution were applied to the surface of the polypropylene filament. An additional sublayer of polymethacrylyl chloride contributed to the strong inoculation of heparin to the polymer. The polymer substrate reacted with heparin to form strong covalent ester bonds. Applying a thin and uniform layer of polyhydroxybutyrate/oxivalerate to the thread with a thickness of no more than 4 microns makes its surface smooth. After chemical modification and application of heparin to the surface of the thread, it acquired a uniform spongy structure, due to the formation of a new polymer layer with firmly grafted heparin. Thus, it is possible to create a bio- and hemocompatible coating based on a biodegradable polymer and heparin on the surface of a polypropylene thread.

Keywords: Surgical suture material, Heparin, Thrombosis, Polypropylene thread, Thrombosis-resistant properties

Introduction

The number of reconstructive operations on various vascular basins is increasing every year in Russia and the world, and in particular, there is a significant increase in arterial reconstructions on the lower extremities [1, 2]. The most common complication of these operations is vascular prosthesis thrombosis – up to 45% [3]. Suture materials in vascular surgery have special requirements. One of the most important requirements is the absence of thread penetration into the lumen of the vessel and its contact with flowing blood [4, 5], however, it is almost impossible to avoid this. In this case, a violation of the integrity of the patient's artery endothelium site in the suture area and the presence of a thread protruding into the lumen of the vessel turn the anastomosis zone into a focus of thrombosis, which is a serious problem in vascular surgery [6-8]. Currently, the suture materials market is represented by various modifications, for example, filaments with antibacterial or anti-inflammatory effects [9-14]. At the same time, there is no suture material with thromboresistant properties in the arsenal of vascular surgeons.

Arterial and venous thrombosis are serious postoperative complications [15, 16]. Approximately 4% of surgical operations are accompanied by the development of venous or arterial thrombosis [17, 18]. There are some factors associated with these complications: atherosclerosis of the coronary arteries in elderly patients, male gender, and a history of venous thromboembolism [19-21]. At the same time, there is a small amount of data indicating the relationship between postoperative thrombosis and infection.

Systemic infections accompanied by inflammation and hypercoagulation may increase the subsequent risk of thrombosis [22, 23]. Moreover, prolonged inflammation is

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associated with an increased risk of myocardial infarction and stroke, as well as deep vein thrombosis and pulmonary embolism [24-27]. It is assumed that hypercoagulation indirectly develops through platelet activation, increased production of fibrin and tissue factors [28-30].

The purpose of this scientific work is to evaluate the possibility of modifying the surface of a polypropylene thread with heparin using chemical inoculation in order to increase the thromboresistant properties of the suture material.

Materials and Methods

In this work, a 3/0 thick polypropylene thread was used. polyhydroxybutyrate/oxivalerate (PHBV) copolymer with a molecular weight of 280 kDa and a solution (0.5%) of unfractionated heparin were used to coat the surface of the thread. For the strong grafting of heparin to the polymer, an additional sublayer of polymethacrylyl chloride was used, chemically grafted to the polymer filament and having active groups in its composition that can react and form strong covalent bonds with heparin. Methacrylyl chloride (methacrylic acid chlorangidride) was used to create it. Purified benzoyl peroxide (BP) or dinitrile azo-bis-isobutyric acid (DAA) was introduced into the modifying solution of PHBV as the initiator of vaccination, in an amount of 2% of the weight of PHBV. Methacrylyl chloride was grafted to PHBV from the gas phase when heated. Inoculation of heparin on the modified surface was carried out from its solution in a bicarbonate buffer at a reduced temperature. After inoculation, the filaments were washed with distilled water and dried in a vacuum over P_2O_5 at room temperature for 2 days.

The inoculation of heparin to the substrate was studied by diffuse scattering spectroscopy using an IR Fourier spectrometer Bruker Vertex 80v (Germany). To increase the area of the test surface of the samples, the modified thread was tightly wound onto a two-layer plate made of thick aluminum foil with dimensions of 0.5x2.0 cm so that a completely closed thread section with dimensions of 0.5x0.5 cm was formed.

The quality of the applied coating was evaluated using scanning electron microscopy (SEM) on a Hitachi-S3400N microscope (Japan).

Results and Discussion

The scientific literature has long described the technologies of radiation-chemical inoculation of heparin to the surface of various polymers in order to increase their hemocompatibility [31-34]. To do this, the polymer substrate was modified by grafted copolymerization with methacrylyl chloride, which subsequently reacted with heparin to form strong covalent ester bonds. However, the radiation method used for this with the help of gamma radiation is technically difficult, unsafe, and unsuitable for large-scale production. The most promising method is the chemical initiation of grafted copolymerization of methacrylyl chloride [35].

Inoculation of the active sublayer, which has active chlorohydride groups in its composition, was carried out by radical inoculation in the presence of initiators (BP or DAA). When heated, these compounds decompose into active radical particles **(Figure 1)**, which react with the polymer matrix (PHBV), dehydrating it to form macroradicals **(Figure 2)**. Subsequently, the macroradicals react with methacrylyl chloride to form a grafted copolymer.

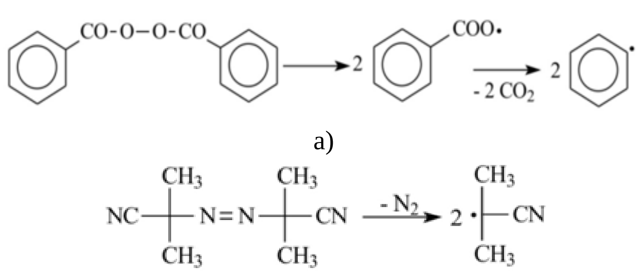


Figure 1. Formation of radicals when heated: a) benzoyl peroxide (BP). b) dinitrile azo-bis-isobutyric acid (DAA)

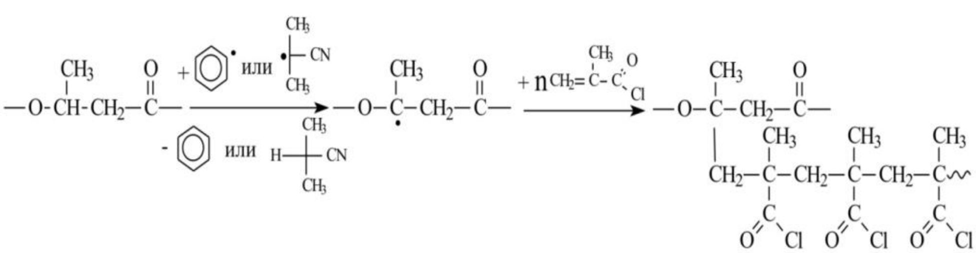


Figure 2. Formation of the grafted copolymer PHBV-methacrylyl chloride

The polymer substrate modified by grafted copolymerization with methacrylyl chloride subsequently reacted with heparin to form strong covalent ester bonds **(Figure 3)**.

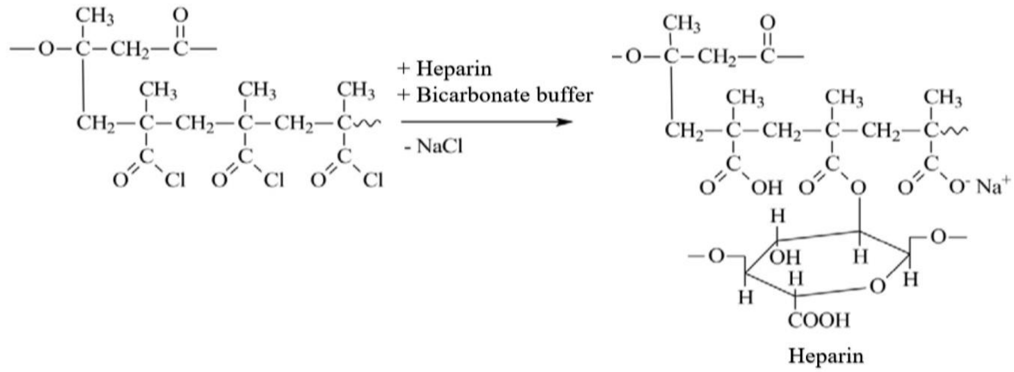


Figure 3. Inoculation of heparin on the surface of a modified polypropylene thread

The inoculation of heparin to the substrate was studied using the diffuse infrared spectroscopy method, which is widely used to study the surface of various objects [36, 37]. This method allows us to obtain reliable information about changes in the composition of the sample surface without adversely affecting it. As can be seen from the above spectrum **(Figure 4)**, a number of differences are observed between the suture material modified with heparin and the original polypropylene thread coated with PHBV, namely:

- an increase in absorption in the region of 3400–3000 cm^{-1}, which is associated with the appearance of a large number of hydroxyl groups of grafted heparin;
- in addition to the general peak at 1740-1720 cm^{-1} (the characteristic peak of the carboxylic ester group of PHBV), new peaks appear at 1696 cm^{-1} - absorption of acid carboxylic groups – COOH of heparin and polymethacrylic acid bound by a hydrogen bond, and a peak at 1637 cm^{-1} – absorption of the carboxylate group – COO^- heparin and polymethacrylic acid.

These differences confirm the inoculation of heparin to the polymer surface. At the same time, both initiators – dinitrile azobisisobutyric acid and benzoyl peroxide – are approximately equivalent in their properties in the inoculation copolymerization reaction.

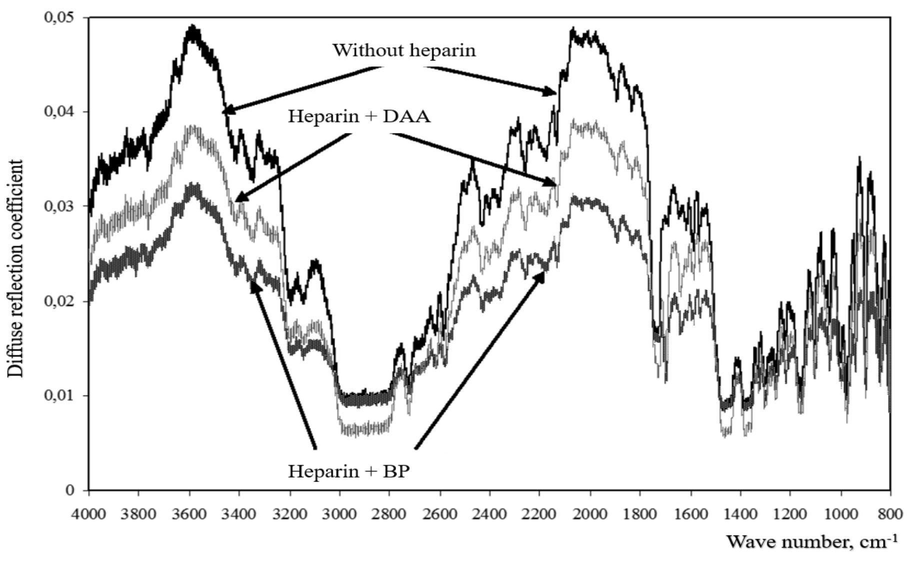
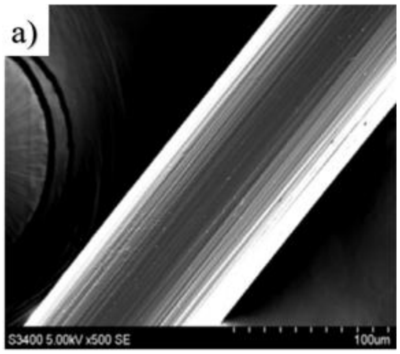
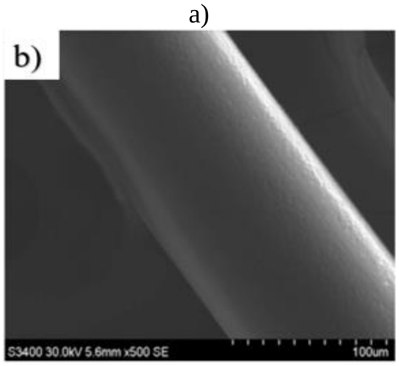


Figure 4. Diffuse reflection spectra of samples of modified suture material in the infrared range

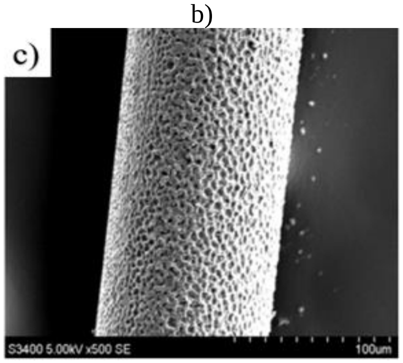
The effect of modification on the surface structure of polypropylene filament was studied by scanning electron microscopy. The surface of the unmodified polypropylene thread has a distinct longitudinal ribbing due to its extraction during molding **(Figure 5a)**. Applying a thin and uniform layer of PHBV to the thread with a thickness of no more than 4 microns makes its surface smooth **(Figure 5b)**. After chemical modification and application of heparin, the surface of the thread acquired a uniform spongy structure **(Figure 5c)**, due to the formation of a new polymer layer with firmly grafted heparin.



a)



b)



c)

Figure 5. Scanning electron microscopy of the suture surface (magnification x500): a) unmodified thread. b) thread + PGBV. c) thread + PGBV + modifying layer + heparin.

Conclusion

Thus, the results obtained demonstrate the prospects of the chosen direction. It is possible to create a bio- and hemocompatible coating based on a biodegradable polymer and heparin on the surface of a polypropylene thread. Applying a thin and uniform layer of polyhydroxybutyrate/oxivalerate to the thread with a thickness of no more than 4 microns makes its surface smooth. After chemical modification and application of heparin to the surface of the thread, it acquired a uniform spongy structure, due to the formation of a new polymer layer with firmly grafted heparin. The technology of chemical inoculation makes it possible to firmly and effectively fix the anticoagulant on the surface of the modified thread, which will help to increase the thrombosis resistance of the suture material.

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References

1. Gantz O, Mulles S, Zagadailov P, Merchant AM. Incidence and cost of deep vein thrombosis in emergency general surgery over 15 years. J Surg Res. 2020;252:125-32. doi:10.1016/j.jss.2020.03.022
2. Hummel T, Aryafar A, Mayböck N, Mumme A, Stücker M, Mühlberger D. Quality of life after varicose vein surgery in patients with high-ligation and stripping, external valvuloplasty and sapheno-femoral redo surgery. Ann Vasc Surg. 2021;74:331-8. doi:10.1016/j.avsg.2020.12.057
3. Cao MT, Higuchi R, Yazawa T, Uemura S, Izumo W, Matsunaga Y, et al. Narrowing of the remnant portal vein diameter and decreased portal vein angle are risk factors for portal vein thrombosis after perihilar cholangiocarcinoma surgery. Langenbecks Arch Surg. 2021;406(5):1511-9. doi:10.1007/s00423-020-02044-1
4. Dresing K, Slongo T. Surgical suture material-fundamentals. Oper Orthop Traumatol. 2023;35(5):298-316. [In German]. doi:10.1007/s00064-023-00812-y
5. Lekic N, Dodds SD. Suture materials, needles, and methods of skin closure: What every hand surgeon should know. J Hand Surg Am. 2022;47(2):160-71. doi:10.1016/j.jhsa.2021.09.019
6. Bartlett MA, Mauck KF, Stephenson CR, Ganesh R, Daniels PR. Perioperative venous thromboembolism prophylaxis. Mayo Clin Proc. 2020;95(12):2775-98. doi:10.1016/j.mayocp.2020.06.015
7. Lin HY, Lin CY, Huang YC, Hsieh HN, Yang YW, Chang IL, et al. Deep vein thrombosis after major orthopedic surgery in Taiwan: A prospective cross-sectional study and literature review. J Formos Med Assoc. 2022;121(8):1541-9. doi:10.1016/j.jfma.2021.12.027
8. Carlin AM, Varban OA, Ehlers AP, Bonham AJ, Ghaferi AA, Finks JF. Independent predictors and timing of portomesenteric vein thrombosis after bariatric surgery. Surg Obes Relat Dis. 2022;18(12):1385-91. doi:10.1016/j.soard.2022.07.016
9. Pesset CM, Fonseca COD, Antunes M, Santos ALLD, Teixeira IM, Ribeiro TAN, et al. Characterizing biofilm formation of Staphylococcus pseudintermedius in different suture materials. Microb Pathog. 2022;172:105796. doi:10.1016/j.micpath.2022.105796
10. Fonticoli L, Diomede F, Nanci A, Fontana A, Della Rocca Y, Guadarrama Bello D, et al. Enriched graphene oxide-polypropylene suture threads buttons modulate the inflammatory pathway induced by Escherichia coli lipopolysaccharide. Int J Mol Sci. 2023;24(7):6622. doi:10.3390/ijms24076622
11. Halepas S, Chen XJ, Ferneini EM. Thread-lift sutures: Anatomy, technique, and review of current literature. J Oral Maxillofac Surg. 2020;78(5):813-20. doi:10.1016/j.joms.2019.11.011
12. Gu Y, Yang J, Yang GZ. Towards occlusion-aware pose estimation of surgical suturing threads. IEEE Trans Biomed Eng. 2023;70(2):581-91. doi:10.1109/TBME.2022.3198402
13. Khalid GM, Billa N. Drug-eluting sutures by hot-melt extrusion: Current trends and future potentials. Materials (Basel). 2023;16(22):7245. doi:10.3390/ma16227245
14. Blinov AV, Nagdalian AA, Povetkin SN, Gvozdenko AA, Verevkina MN, Rzhepakovsky IV, et al. Surface-oxidized polymer-stabilized silver nanoparticles as a covering component of suture materials. Micromachines (Basel). 2022;13(7):1105. doi:10.3390/mi13071105
15. Fawzy H, Hendawy D, Ghareeb M, Amer M, Sameh H, Mosaad H. The value of plasma mir 126 and miR 423-3p levels in the prediction of subclinical atherosclerotic coronary artery disease. J Med Pharm Chem Res. 2024;6(5):609-22. doi:10.48309/jmpcr.2024.428610.1050
16. Whiteley W, Wood A. Risk of arterial and venous thromboses after COVID-19. Lancet Infect Dis. 2022;22(8):1093-4. doi:10.1016/S1473-3099(22)00314-0
17. Borhani-Haghighi A, Hooshmandi E. Cerebral venous thrombosis: A practical review. Postgrad Med J. 2024;100(1180):68-83. doi:10.1093/postmj/qgad103

18. Baranga L, Khanuja S, Scott JA, Provancha I, Gosselin M, Walsh J, et al. In situ pulmonary arterial thrombosis: Literature review and clinical significance of a distinct entity. AJR Am J Roentgenol. 2023;221(1):57-68. doi:10.2214/AJR.23.28996
19. de Winter MA, Dorresteijn JAN, Ageno W, Ay C, Beyer-Westendorf J, Coppens M, et al. Estimating bleeding risk in patients with cancer-associated thrombosis: Evaluation of existing risk scores and development of a new risk score. Thromb Haemost. 2022;122(5):818-29. doi:10.1055/s-0041-1735251
20. Tang G, Qi L, Sun Z, Liu J, Lv Z, Chen L, et al. Evaluation and analysis of incidence and risk factors of lower extremity venous thrombosis after urologic surgeries: A prospective two-center cohort study using LASSO-logistic regression. Int J Surg. 2021;89:105948. doi:10.1016/j.ijsu.2021.105948
21. Peng G, Wang Q, Sun H, Gan L, Lu H, Deng Z, et al. Development and prospective validation of a novel risk score for predicting the risk of lower extremity deep vein thrombosis among multiple trauma patients. Thromb Res. 2021;201:116-22. doi:10.1016/j.thromres.2021.02.020
22. Pastori D, Cormaci VM, Marucci S, Franchino G, Del Sole F, Capozza A, et al. A comprehensive review of risk factors for venous thromboembolism: From epidemiology to pathophysiology. Int J Mol Sci. 2023;24(4):3169. doi:10.3390/ijms24043169
23. Setyawati AN. The role of oxidative stress in hypoalbubimenia nephropathy related to Nephrotic syndrome: A critical review. J Med Pharm Chem Res. 2024;6(1):32-49. doi:10.48309/jmpcr.2024.182755
24. Andreotti F, Massetti M, Montalescot G. Thrombosis, bleeding, and the promise of factor XI(a) inhibition. J Am Coll Cardiol. 2024;83(6):679-81. doi:10.1016/j.jacc.2023.12.003
25. Rubino R, Imburgia C, Bonura S, Trizzino M, Iaria C, Cascio A. Thromboembolic events in patients with influenza: A scoping review. Viruses. 2022;14(12):2817. doi:10.3390/v14122817
26. Khan SU, Agarwal S, Arshad HB, Akbar UA, Mamas MA, Arora S, et al. Intravascular imaging guided versus coronary angiography guided percutaneous coronary intervention: Systematic review and meta-analysis. BMJ. 2023;383:e077848. doi:10.1136/bmj-2023-077848
27. Bai M, Lu A, Pan C, Hu S, Qu W, Zhao J, et al. Veno-arterial extracorporeal membrane oxygenation in elective high-risk percutaneous coronary interventions. Front Med (Lausanne). 2022;9:913403. doi:10.3389/fmed.2022.913403
28. Asmis L, Hellstern P. Thrombophilia testing - A systematic review. Clin Lab. 2023;69(4). doi:10.7754/Clin.Lab.2022.220817
29. Lauridsen SV, Hvas CL, Sandgaard E, Gyldenholm T, Mikkelsen R, Obbekjær T, et al. Thromboelastometry shows early hypercoagulation in patients with spontaneous subarachnoid hemorrhage. World Neurosurg. 2019;130:e140-9. doi:10.1016/j.wneu.2019.06.019
30. Marlar RA. Laboratory evaluation of thrombophilia. Methods Mol Biol. 2023;2663:177-201. doi:10.1007/978-1-0716-3175-1_10
31. Raman K, Arungundram S. Chemical approaches to prepare modified heparin and heparosan polymers for biological studies. Methods Mol Biol. 2022;2303:289-96. doi:10.1007/978-1-0716-1398-6_23
32. Qian Y, Zhang J, Xu R, Li Q, Shen Q, Zhu G. Nanoparticles based on polymers modified with pH-sensitive molecular switch and low molecular weight heparin carrying Celastrol and ferrocene for breast cancer treatment. Int J Biol Macromol. 2021;183:2215-26. doi:10.1016/j.ijbiomac.2021.05.204
33. Kocak FZ, Yar M, Rehman IU. Hydroxyapatite-integrated, heparin- and glycerol-functionalized chitosan-based injectable hydrogels with improved mechanical and proangiogenic performance. Int J Mol Sci. 2022;23(10):5370. doi:10.3390/ijms23105370
34. Gupta S, Puttaiahgowda YM, Deiglmayr L. Recent advances in the design and immobilization of heparin for biomedical application: A review. Int J Biol Macromol. 2024;264(Pt 2):130743. doi:10.1016/j.ijbiomac.2024.130743
35. Mahmood DA, Kareem MM, Witwit IN. New n-substituted itaconimide polymers: Synthesis, characterization, and biological activity. J Med Pharm Chem Res. 2023;5(9):866-84.
36. Giubertoni G, Rombouts G, Caporaletti F, Deblais A, van Diest R, Reek JNH, et al. Infrared diffusion-ordered spectroscopy reveals molecular size and structure. Angew Chem Int Ed Engl. 2023;62(2):e202213424. doi:10.1002/anie.202213424
37. Caggiani MC, Occhipinti R, Finocchiaro C, Fugazzotto M, Stroscio A, Mazzoleni P, et al. Diffuse reflectance infrared fourier transform spectroscopy (DRIFTS) as a potential on-site tool to test geopolymerization reaction. Talanta. 2022;250:123721. doi:10.1016/j.talanta.2022.123721