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# Creation of a Novel Surgical Suture Material Designed to Inhibit Arterial Thrombosis Formation

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## Abstract

Thrombosis of vascular prostheses is one of the most important complications following surgical procedures on the lower extremity arteries. Unfortunately, preventing the surgical thread from interacting with flowing blood is nearly impossible, which makes the surgical site prone to thrombosis. This study aimed to investigate the potential for increasing the thromboresistance of polypropylene suture material by modifying its surface with heparin through chemical inoculation. To achieve this goal, a solution of heparin was applied to the polypropylene filament's surface, along with a polyhydroxybutyrate/oxivalerate copolymer. A polymethacrylyl chloride underlayer was introduced to ensure the strong bonding of heparin to the polymer. The polymer reacted with heparin, creating durable covalent ester bonds. A smooth surface was achieved by applying a thin polyhydroxybutyrate/oxivalerate layer no thicker than 4 microns. After undergoing chemical modification and heparin application, the filament developed a uniform, spongy texture, resulting from a newly formed polymer layer with securely attached heparin. This process opens the possibility of creating a bio- and hemocompatible coating based on a biodegradable polymer and heparin for use on the surface of polypropylene sutures.

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

## Introduction

The number of reconstructive vascular procedures, particularly involving the arteries of the lower limbs, continues to grow both in Russia and globally [1, 2]. A major postoperative complication associated with these interventions is thrombosis of the vascular prosthesis, with incidence rates reported as high as 45% [3]. Vascular surgery demands specific properties from suture materials, among which the prevention of thread intrusion into the vessel lumen and contact with circulating blood is paramount [4, 5]. However, achieving complete avoidance of such contact remains extremely difficult. When the endothelial lining of the arterial wall is disrupted at the suture site and the thread protrudes into the vessel interior, the anastomosis becomes a prime site for thrombus formation—a challenge that significantly complicates vascular surgical outcomes [6–8].

Despite a variety of modern suture materials on the market, including those engineered with antibacterial or anti-inflammatory properties [9–14], none are currently designed to resist thrombosis, leaving a critical gap in surgical practice. Both venous and arterial thrombosis are recognized as severe complications following surgery [15, 16], and data suggests that nearly 4% of operations result in such thrombotic events [17, 18]. Factors like advanced age with coronary artery disease, male sex, and prior venous thromboembolism are recognized contributors to these outcomes [19–21]. While there is limited information directly linking postoperative thrombosis to infectious processes, existing studies suggest that systemic infections marked by inflammation and hypercoagulability may increase the risk of thrombus development [22, 23].

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Chronic inflammatory states further elevate the likelihood of cardiovascular incidents such as myocardial infarction, stroke, deep vein thrombosis, and pulmonary embolism [24–27]. The underlying mechanism is thought to involve enhanced platelet activity, elevated fibrin production, and upregulation of tissue factors, collectively promoting a hypercoagulable environment [28–30].

This study seeks to assess the feasibility of chemically modifying the surface of polypropylene suture threads by grafting heparin through inoculation techniques, to enhance their thromboresistant characteristics.

## Materials and Methods

In this study, polypropylene suture material with a thickness of 3/0 was utilized as the base. To modify its surface, a polyhydroxybutyrate/oxivalerate (PHBV) copolymer with a molecular weight of 280 kDa and a 0.5% solution of unfractionated heparin were applied. For secure heparin attachment, a supplementary polymethacrylyl chloride sublayer was incorporated. This intermediate layer, chemically bonded to the polymer filament, contained reactive functional groups capable of forming durable covalent linkages with heparin. Methacrylyl chloride (also known as methacrylic acid chlorangidride) was employed to generate this reactive sublayer. The initiation of grafting was facilitated by the inclusion of purified benzoyl peroxide (BP) or dinitrile azo-bis-isobutyric acid (DAA) into the PHBV solution, serving as initiators at a concentration of 2% relative to the polymer's mass. Methacrylyl chloride was introduced in vapor form during thermal treatment to ensure effective binding to PHBV. The grafting of heparin onto the chemically modified surface was executed using a bicarbonate buffer solution under low-temperature conditions. Post-grafting, the threads were thoroughly rinsed with distilled water and subsequently vacuum-dried at ambient temperature over phosphorus pentoxide ($P_2O_5$) for 48 hours.

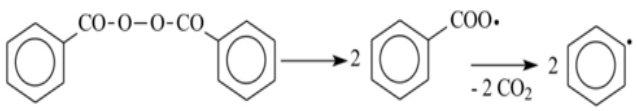
The effectiveness of heparin grafting onto the polymer substrate was analyzed through diffuse reflectance infrared spectroscopy, conducted with a Bruker Vertex 80v IR Fourier spectrometer (Germany). To maximize the surface area for spectral analysis, the treated threads were carefully wound around a dual-layer aluminum foil plate measuring 0.5 × 2.0 cm, creating a fully enclosed area of 0.5 × 0.5 cm.

Assessment of the surface coating quality was carried out using scanning electron microscopy (SEM), employing the Hitachi-S3400N instrument (Japan).

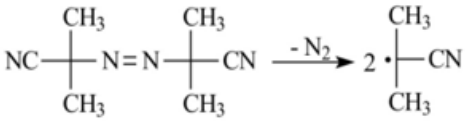
## Results and Discussion

The use of radiation-chemical methods for grafting heparin onto polymer surfaces to enhance hemocompatibility has been documented extensively in scientific sources [31–34]. These approaches typically involve modifying the polymer base through graft copolymerization with methacrylyl chloride, which subsequently interacts with heparin to establish durable covalent ester bonds. However, the conventional technique involving gamma radiation presents considerable limitations—it is complex, poses safety risks, and is impractical for application in industrial-scale manufacturing. In contrast, the chemical initiation of methacrylyl chloride graft copolymerization has emerged as a more viable and efficient alternative [35].

The application of an active sublayer containing chlorohydride functional groups was achieved via radical-based grafting using initiators such as benzoyl peroxide (BP) or dinitrile azo-bis-isobutyric acid (DAA). Upon thermal activation, these initiators decompose into highly reactive radicals **(Figure 1)**, which subsequently interact with the polymer matrix—specifically PHBV—by extracting hydrogen atoms, thereby producing macroradicals **(Figure 2)**. These macroradicals then undergo a reaction with methacrylyl chloride, resulting in the formation of a grafted copolymer structure.




a)



b)

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

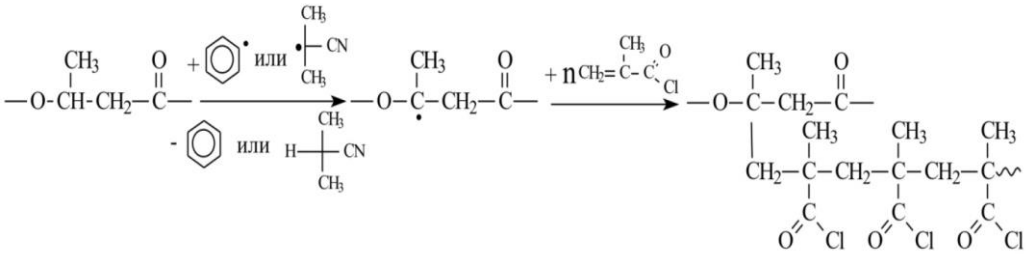


**Figure 2.** Formation of the grafted copolymer PHBV-methacrylyl chloride

Following graft copolymerization with methacrylyl chloride, the altered polymer substrate underwent a chemical reaction with heparin, leading to the formation of stable covalent ester linkages (**Figure 3**).

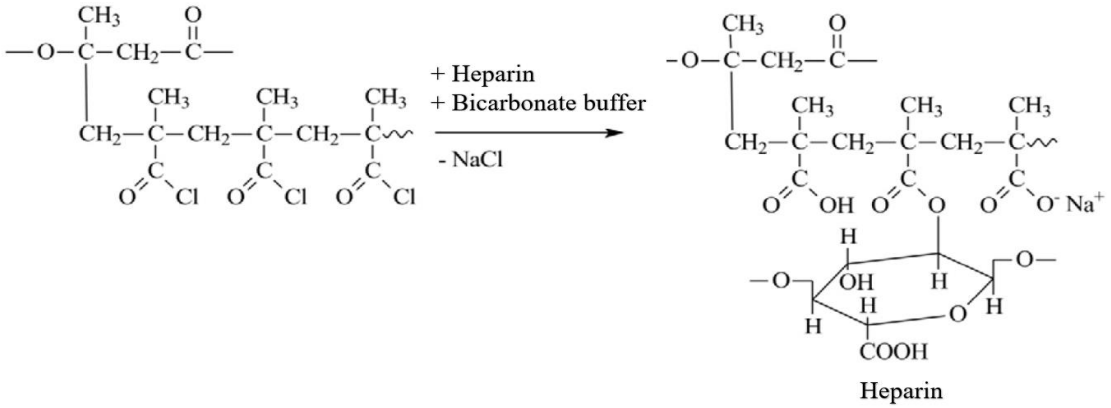



**Figure 3.** Inoculation of heparin on the surface of a modified polypropylene thread

To evaluate the grafting of heparin onto the polymer substrate, diffuse infrared spectroscopy was employed—a well-established analytical technique for assessing surface composition across a wide range of materials [36, 37]. This non-destructive method enables accurate detection of surface chemical modifications without altering the structural integrity of the sample. Analysis of the obtained spectrum **(Figure 4)** reveals several distinguishing spectral features when comparing the heparin-modified suture to the unmodified polypropylene thread coated with PHBV:

- A noticeable rise in absorption within the 3400–3000 $cm^{-1}$ range, attributed to the emergence of numerous hydroxyl groups introduced by the grafted heparin;
- In addition to the prominent peak at 1740–1720 $cm^{-1}$—typical of the carboxylic ester group present in PHBV—new signals appear at 1696 $cm^{-1}$, corresponding to the vibrational absorption of carboxylic acid groups (COOH) from heparin and hydrogen-bonded polymethacrylic acid, and at 1637 $cm^{-1}$, indicating the presence of carboxylate anions ($COO^-$) derived from both heparin and polymethacrylic acid.

These spectral changes validate the successful grafting of heparin onto the polymer surface. Furthermore, both initiators used in the grafting process—dinitrile azobisisobutyric acid and benzoyl peroxide—demonstrated similar efficacy in initiating the copolymerization reaction.

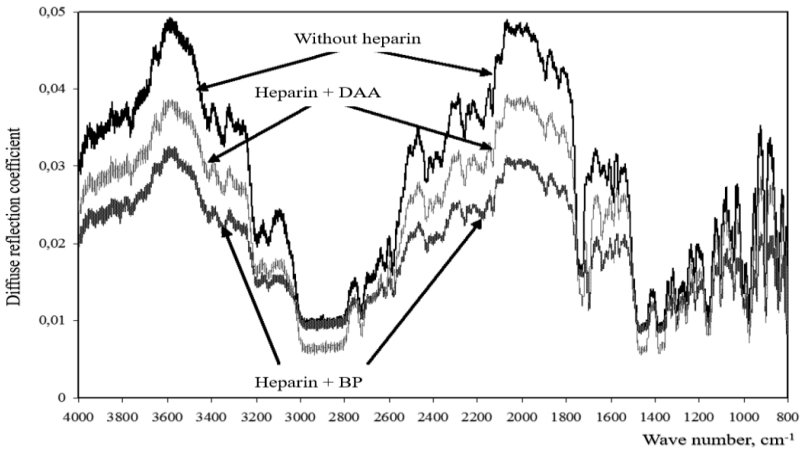
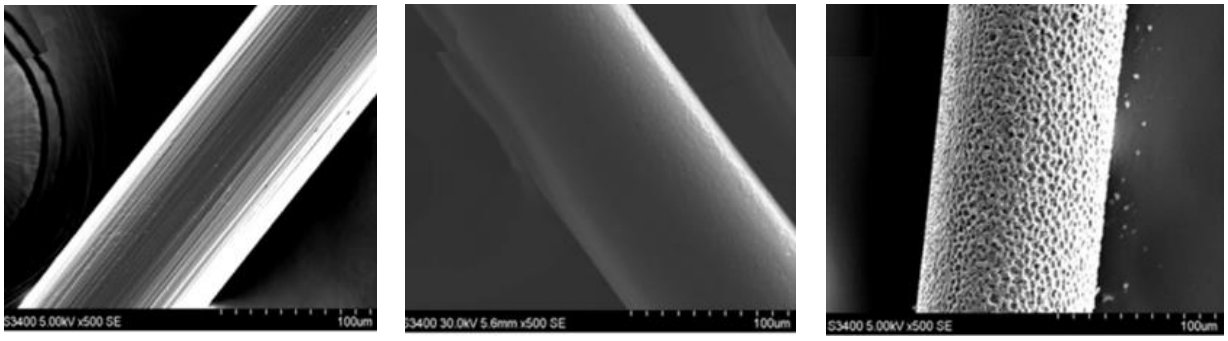



**Figure 4.** Diffuse reflection spectra of samples of modified suture material in the infrared range

The influence of surface modification on the structural characteristics of polypropylene filament was examined using scanning electron microscopy. Initially, the untreated polypropylene thread exhibited pronounced longitudinal grooves, which are typical artifacts resulting from the extrusion process during molding **(Figure 5a)**. The application of a thin, even coating of PHBV—measuring less than 4 microns in thickness—eliminated these ridges and rendered the surface smooth and uniform **(Figure 5b)**. Following subsequent chemical modification and heparin integration, the surface morphology of the filament transformed into a consistently porous, sponge-like texture **(Figure 5c)**, indicating the successful formation of a new polymeric layer with securely bonded heparin.




a) b) c)

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

## Conclusion

The findings of this study highlight the viability of the selected approach for enhancing suture materials. A biocompatible and hemocompatible surface layer can be developed by incorporating heparin into a biodegradable polymer matrix applied to polypropylene threads. Coating the thread with a thin film of polyhydroxybutyrate/oxivalerate, no thicker than 4 microns, leads to a visibly smoother surface. Subsequent chemical treatment and heparin grafting result in the formation of a consistent, sponge-like outer layer, which

reflects the successful integration of a new polymer structure containing firmly bonded heparin. This chemically induced grafting technique offers a reliable method for anchoring anticoagulant agents to the thread surface, potentially improving the thromboresistant characteristics of the surgical suture material.

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**Conflict of Interest:** None

**Financial Support:** None

**Ethics Statement:** None

**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