Electronic Journal of General Medicine
2023, 20(6), em538
e-ISSN: 2516-3507
https://www.ejgm.co.uk/

MODESTUM

Review Article **OPEN ACCESS**

New and more effective application assays for hemostatic disorder assessment: A systematic review

Faisal M Al-Zahrani [1]*

[1] Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, Imam Abdulrahman Bin Faisal University, Dammam, SAUDI ARABIA
***Corresponding Author:** fmzahrani@iau.edu.sa

Citation: Al-Zahrani FM. New and more effective application assays for hemostatic disorder assessment: A systematic review. Electron J Gen Med. 2023;20(6):em538. https://doi.org/10.29333/ejgm/13570

ARTICLE INFO

Received: 23 May 2023

Accepted: 18 Jul. 2023

ABSTRACT

Background: Hemostasis research lacked novel platform assays for hemostatic disorder diagnosis. The current review study's goal is to compare various assays for evaluating the novel hemostatic techniques used in the diagnosis of coagulation disturbances and to highlight each method's strongest and weakest points.

Methods: The PRISMA guidelines and the recommendations for observational studies in epidemiology were both followed in the current systematic review. The PRISMA-compliant electronic databases (PubMed), a novel platform for evaluating hemostasis, were searched using the keywords. The electronic databases (PubMed), a cutting-edge platform to assess hemostasis, were searched using the keywords. Articles published between December 2016 and December 2021 were only included in searches; original articles were written in English. In order to assess hemostasis studies, we gathered bibliographies of abstracts that were published on the new and more effective application assays for assessments of hemostasis disorders.

Results: Following the removal of duplicates, articles were determined by examining the titles and abstracts. Disagreements were resolved through consensus and the application of novel hemostatic analysis methods. Then independently reviewed the relevant studies of the recognized records (n=503), excluding duplicates (n=9) and irrelevant studies (n=249). The remaining 254 studies were read in their entirety, the data from the seven included studies had been extracted.

Conclusions: When expressed as an anticoagulant for the in vivo assessment of on the complement system, nanotechnology-based study was more effective in some laboratory tests, and flow cytometer evaluation could be a promising platform approach for use in hemostasis management.

Keywords: novel platform, hemostasis assays, diagnosis, hemostatic disorders

INTRODUCTION

Novel platform assays for the diagnosis of hemostatic disorders were limited in hemostasis research during the drug acceleration phase of vitro-based therapeutics, particularly during the product design phase. An in vitro test flow was built in the year 2005 to evaluate the immune response stability of nanomaterials and devices for hemostatic evaluations [1]. 400 different nanotechnology devices were used to validate the hemostasis biomarker sequence. In addition to liposomes, emulsified, nanostructured lipid carriers, colloidal metals, metal oxides, nanotubes, fullerenes, and polymeric nanotechnology were also taken into consideration. To prevent the blood clotting of the healthy donated blood used in such lab tests, a few assays were carried out using either traditional anticoagulants or hirudins. Earlier, a novel T2 magnetic resonance-based method for measuring hemostasis in whole blood was described (T2MR) [2]. One such method has a small blood volume requirement (35 l), is essentially straightforward because platelets are not really separated, and yields results quickly. Fibronectin is essential for healing, bacteria-host interaction, and adhesion strength. Lower serum fibronectin levels have been suggested in some studies as a potential disease risk factor for the development of anti-PF4 and anti-heparin antibodies and professional HIT. In addition, fibronectin inhibited the formation of PF4 and PF4/heparin complexes on extracted platelets, complex disruption, downregulation of antibodies with high affinity for PF4/heparin complexes, and decreased expression of anti-PF4/heparin antibody-induced immune activation. These effects were all brought about by fibronectin. In addition, the Scientific and Standardization Committee of the International Society on Thrombosis and Hemostasis orders flow cytometer processing as more than just a method of processing when compared to routine diagnostic disorders, and it is demonstrated to be preferred to light transmission aggregometry throughout the diagnosis and treatment of platelet activity dysfunction [5, 6]. Even in the flow cytometer testing of mild routine diagnostic disorders, platelet granule identifiers, such as p-selectin, are used; however, platelet stimulation must occur prior to the analysis. The fluorescence-functionalized subset, which connects receptor nuclei, is frequently used to estimate platelet density. Reduced mepacrine fluorescence has been identified in patients with storage pool disorder (SPD) by several researchers [7, 8], and it is suggested that this finding

be incorporated into a screening methodology for common diagnostic disorders. It remains to be seen whether ongoing fluorescent records will be successful in a real-world medical setting, especially when compared to customary SPD screening procedures [9, 10]. Oceans are abounding with natural resources. A crucial aspect of aquatic active ingredient analysis would be the fact that many marine products are made from naturally occurring active ingredients with specific properties, including marine-appropriate peptides. Marine active peptides have been found to have antimicrobial, hemostatic, and wound-healing properties [11-13]. In order to transform enzyme inhibitor peptides and antioxidant peptides, oyster peptides (OP), which are active substances present in marine organisms, include angiotensin I and antiseptic peptides [14, 15]. In studies, it has been shown to have exceptional biological properties, including antibacterial, antioxidant, hypoglycemic, anti-aging, and anti-tumor activity [16, 17]. OP too has typical physical and chemical properties, such as various compositions, ease of adaptation, and non-toxic and non-harmful properties [14, 15]. Besides that, because of their readily available nutrition and poor bio stability, they are exposed to microorganism invasion, resulting in the loss of biological processes [18]. Platelet abnormalities should always be monitored in order to diagnose mild bleeding disorders, which are characterized by grossly disproportionate bleeding after trauma, menorrhagia, severe and frequent mucocutaneous hemorrhage, and easy bruising [19, 20]. Although this technique has been used in diagnostic laboratories for more than four decades, it still lacks sensitivity for mild platelet function defects (PFDs) and does not predict the risk of bleeding health problems in patients with certain clinical diagnostic defects [21-26]. The difficulties of transmission aggregometry may include poor standardization, but besides existing guidelines, the need for a large amount of fresh blood, the realization that it is periodical and time-consuming, and that it is not applicable for analyzing platelet count [27-32]. As a result, alternative techniques for measuring platelet aggregation have just been developed, but despite potential advantages, neither of these techniques raced with light transmission aggregometry (LTA) in terms of bleeding diagnostics [33]. Alternative methods for providing additional data about mild PFDs are desperately needed. The whole normal platelet initiation test, developed by [34], is a flow cytometric approach that enables platelets to just be stimulated with various agonists and platelet stimulation to be quantified using different kinds of activation markers such as granule official launch, glycoprotein activation, and phospholipid expression. Because many research laboratories do not have both aggregometry and flow cytometer capabilities, records based on the agreed methodologies are as previously published [35, 36]. Using synthetic and natural polymers such as chitosan, electro spinning allows us to create three-dimensional porous and fibrous materials [37]. This method is used in biomedicine and tissue engineering in conjunction with 3D printing [38]. While the extracellular matrix is modeled by electrode position scaffolds for rapid cell proliferation and tissue regeneration [39], early literature has shown that electro-spun chitosan membranes have high blood clot-forming activity as well as biocompatibility. Furthermore, the composition of hydrogen bonds formed after chitosan dissolves in an acid solution complicates the spinning process, limiting the use of pure chitosan [40]. Extra added polymers, like caprolactone (PCL), polyvinyl alcohol (PVA), or polyethylene oxide (PEO), are now used to improve chitosan spinning, reduce conductivity, or produce thinner fibers [41]. The best way to stabilize the chitosan electroprocessing route would have been to add PEO, a water-soluble synthetic polymer with good biocompatibility and low toxicity [42]. In a previous study, PEO was used, which binds to chitosan via hydrogen bonds, lowering the viscosity and interfacial of the chitosan solution. The purpose of the present review study would be to make a comparison between several assays for assessing the novel hemostatic techniques used in the diagnosis of coagulation disturbance and to point out the most advantageous and disadvantageous aspects of each method as a predictor of morbidity and mortality to determine hemostatic efficacy as well as biological safety.

METHODS

Study Selection

The current systematic review follows the guidelines for observational studies in epidemiology [8] and the PRISMA guidelines. **Figure 1** depicts a high-level overview of the methodology. The keywords were used to search the electronic databases (PubMed) (a novel platform to evaluate hemostasis). Searches were restricted to articles published between December 2016 and December 2021; original articles were written in English. To summarize, we collected bibliographies of abstract articles published on a novel platform to evaluate laboratory techniques used for hemostasis studies, and no attempt was made to contact the original article's authors for information. This study does not require ethical approval because the included data is based on previously reported articles, and no identifying information about participants will be revealed. IBM (IBM Corp., USA) software was used for statistical analysis in this study.

RESULTS

Following the removal of duplicates, articles were determined by examining the titles and abstracts. Conflicts were settled through consensus and the use of novel hemostatic analysis methods. The relevant studies of the recognized records (n=503) were reviewed, excluding duplicates (n=9) and irrelevant studies (n=249). The remaining 254 studies were read in all of them, and data from the seven included studies were extracted (**Figure 1** represents the search strategy and screening procedures). The incidence rate of new platforms to analyze hemostasis is summarized in **Table 1** for the reported studies. The total number of patients considered in the present review (seven studies) was 216, with an absolute max of 161 patients and a minimum of 0.01, as follows: fibronectin modulates formation (n=42), T2 magnetic resonance (n=1), electrospun chitosan-based (n=2), flow cytometric mepacrine fluorescence (n=3), chitosan-based thermo-sensitive (n=1), and nanotechnology-based formulation. The benefits of nanotechnology-based formulations as a novel platform would be optimal in vitro assays demonstrating anticoagulant for nanoparticle effects on the complement system, but less ideal and would require emphasis in test results dependent on the specific anticoagulant being used. While the flow cytometric analytical method has been used for many different measurements, specific, small amounts of blood have been required for such

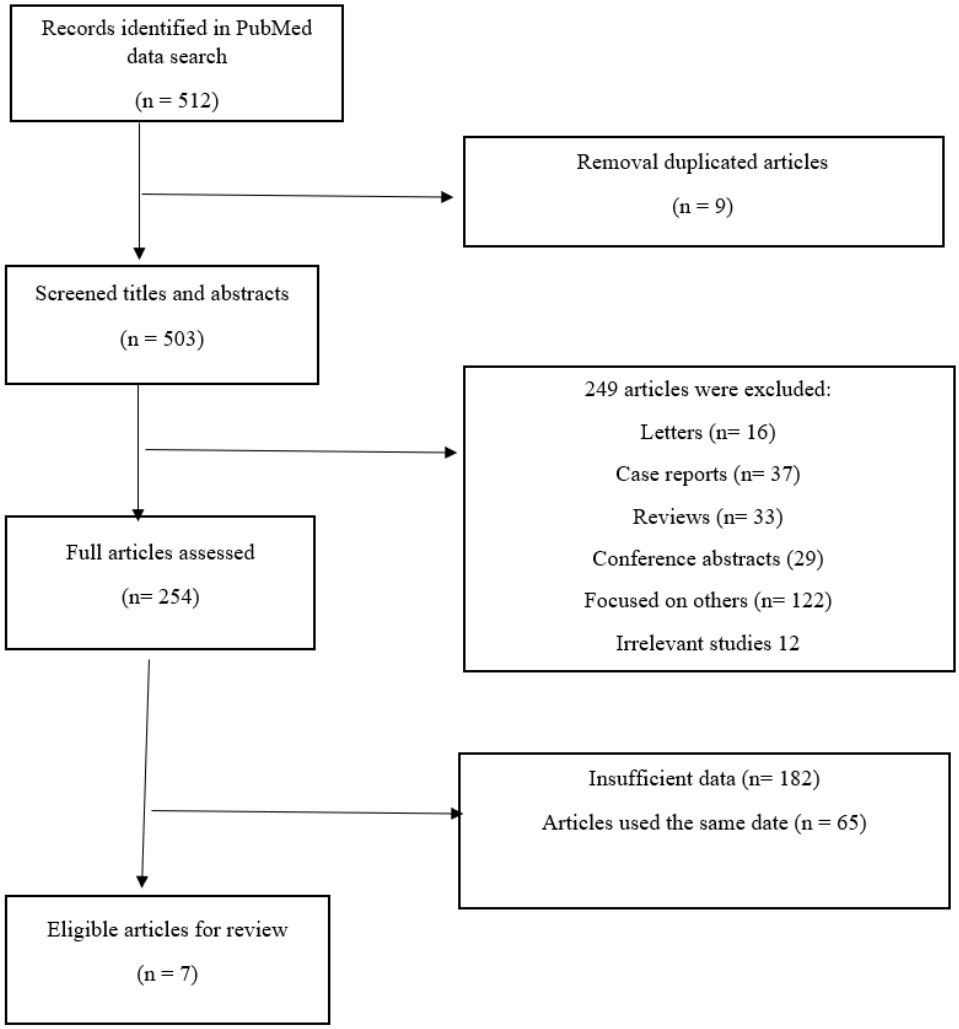

Figure 1. Preferred reporting studies for systematic reviews (Source: Author's own elaboration)

Table 1. The estimated prevalence of a new platform for analyzing hemostasis in the studies investigated

Novel platform	Study	No. of Patients	Positive (%)	Negative (%)
Fibronectin modulates formation	[43]	*42*	*18*(42.8)	*24*(57.2)
T2 Magnetic Resonance	[44]	*1*	*1*(100)	*0*(0.00)
Electrospun Chitosan-Based	[45]	*2*	*2*(100)	*0*(0.00)
Flow cytometric mepacrine fluorescence	[46]	*3*	*3*(100)	*0*(0.00)
Chitosan-Based Thermo-Sensitive	[47]	1	1(100)	0(0.00)
Nanotechnology-Based Formulations	[48]	6	5(83.3)	1(16.7)
Flow cytometric analysis	[49]	161	116(72.0)	45(28.0)

tests but depended on skilled personnel, increased cost, short-time reagents, complicated samples, low sensitivity tests, and short-term indicator molecules. While T2 magnetic resonance might indeed enable the identification of platelet disorders in whole blood to extend to assessments of hemostasis, it even had some disadvantages in basic analytic techniques. Other novel platforms for evaluating hemostasis used in the current studies may require further evaluation to determine their benefits and drawbacks in hemostasis assessment (**Table 2**).

DISCUSSION

Observing the mechanical and physical properties of clotting blood is perhaps the most effective method for monitoring blood coagulation. In fact, the formation of blood clots is monitored in order to prevent platelet aggregation from interfering with the coagulation process [50, 51]. Coagulation can also be caused by an individual's inner stimulation reagent, including ellagic acid or phospholipid [52], an extrinsic inducer solution, such as tissue factor [53], or all of these can be triggered by clotting inhibitors, such as cytochalasin D in combination with an exterior activator [54]. Previous analyses [55, 56] evaluated various point-of-care (POC) devices for test results but instead briefly described their scanning principles, although this systematic looked into other blood clotting checking methodologies. Experimental measurements of various technologies can provide biologists with ideas on the obvious benefits of certain tools in identifying disorders and future performance for clinical management and treatments. Furthermore, the role of nanotechnology in detection and diagnosis, as well as commonly available devices, future trends in checking of novel treatments, artificial intelligence in diagnostic testing, and monitoring for greater predictive value

Table 2. The advantages and disadvantages of a new platform for evaluating hemostasis

Method platform	Advantages	Disadvantages
Fibronectin modulates formation	The decline in fibronectin leads to an increase in PF4, potentially immunizing PF4/heparin complexes in heparin-treated patients.	Fibronectin inhibits platelet activation by anti-PF4/heparin antibodies by interfering with the formation of PF4/heparin complexes.
T2 Magnetic Resonance	T2MR may subsequently facilitate the identification and identification of platelet disorders in whole blood, extending to global haemostatic assessments.	Basic and clinical research is required to determine that whether latest technique will provide a more biological systems and quantifiable measure of poor platelet activation.
Electrospun Chitosan-Based	Particles with significantly higher porosity also show high biocompatibility and adequate in vitro blood clotting blood interaction.	The application really wasn't useful for parenchymal bleeding because it had a lower immunogenicity with an acceptable host-tissue response.
Flow cytometric mepacrine fluorescence	It has the ability to be used in the testing of platelet dense granules.	It is not a quick screening and contains a low amount of whole blood.
Chitosan-Based Thermo-Sensitive	It rapidly takes up water and stays focused on blood, resulting in extremely rapid platelet aggregation, which can be used to identify patients with severe laboratory tests.	The safety evaluations required to ensure the specific hemostasis pathways remain a significant challenge.
Nanotechnology-Based Formulations	In vitro analysis has shown that nanoparticles have anticoagulant consequences on the signaling pathway.	It's much less ideal but also necessary to distinguish differences throughout findings depending on the nature of the anticoagulant in use.
Flow cytometric analysis	So several various measurements were recorded with this device, and only a smaller amount is required for the test.	Short-term reagents, processing conditions, higher sensitivity check, short-term highlighter molecule, specialized workers, and higher prices

have both been explained. As a result, both industrial and academic parts have been enclosed, allowing for the filling of present gaps in blood coagulation monitoring as well as new plans for prolonged hemostasis monitoring. HIT Serum monitoring research of heparin-treated patient population's shows that only a subset of patients develops platelet-activating anti-PF4/heparin antibodies [57, 58] another initially described a novel T2 magnetic resonance platform for measuring hemostasis for whole blood (T2MR) requires small blood (35 lL), and was indeed basically simple, but since platelets are not separated, it actually works in minutes [2]. As a result, the aim of this systematic review would be to contrast certain novel methods for evaluating hemostasis and platelet advantages and disadvantages of this platform for evaluating blood clotting [8, 59]. Another request was made to assess the biocompatibility and hemostatic and tissue properties by using the regeneration performance of copolymers prepared by electro spinning technique in order to develop new techniques to reduce the biodegradation time of their based material properties for hemostatic application. Flow cytometer fluorescence is being used to rule out platelet dense granule shortage, but this test is time-consuming and requires a large blood volume [60]. It can also be used for the analysis of platelets as a potential alternative, but it lacks confirmation, preventing it from being used in a diagnostic setting [61]. Another of the leading causes of death in trauma emergency cases is unregulated massive hemorrhage. At a specific temperature, chitosan-based thermo-sensitive hydrogel loading OP was prepared using catechol-modified chitosan (CS-C) as the matrix material as a thermo-sensitive agent. Hemostasis performance has been measured in vivo and in vitro, as well as its biological safety. The findings revealed that hemostasis experiments, the hemostasis time, and indeed the amount of blood loss in post-operative models were improved due to the small quantities of nano-materials usable for such studies. In vitro analysis of novel nanotechnology-based pharmaceutical formulations is of vital importance, particularly during the product development phase. Almost all immune tests necessitate the use of blood donors [61]. To perform such test results, blood must be kept from coagulating, which itself is an attachment, by adding an anticoagulant to blood testing tubes. The most widely used anticoagulants are heparin, ethylene diamine tetra acetic acid, and citrate [62]. New anticoagulants, including hirudin, are also available but rarely used. Although certain anticoagulants may influence assay results, there is currently very little systematic correlation of traditional and novel anticoagulants in in vitro experiments aimed at immunological identification of nano medicine formulations, whereas traditional anticoagulants, such as citrate and heparin, are more relevant for coagulation and cytokine secretion assays. The research suggests that this technology is likely to be favorable mostly in the medical field of hemostasis, and those variations in lab tests between and traditional mechanisms involving blood for nanostructures have all been observed at a time when no such results were observed with traditional controls [63]. As a result, it is critical to understand the benefits and drawbacks of each anticoagulant and to establish appropriate nanoparticles on a case-by-case basis. Introduction LTA has been the gold standard for identifying bleeding disorders and might be useful in standardizing diagnostic work-up studies. A parameter estimation that excluded single studies had no effect on the significance of this association. Several limitations of the research must be considered carefully. First, our findings are useful because of confounding factors such as patient clinical characteristics, sample size, and hemostatic defect estimation procedure [1, 62]. The aforementioned confounders, on the other hand, fully described the observed. As a result, some authors suggested that some studies have not been provided, and we have had to estimate the value based on the data. There may be small variations between the precise methodology used and the extrapolated data obtained using the laboratory method. Despite the fact that we did not impose a language restriction, only studies in English were included in the review. Subsequently, studies with insufficient data have been omitted. Besides this, several additional studies were unable to be published due to negative or null results; these studies were, in fact, excluded from the current analysis. Each of these factors could have contributed to the limitations observed in this review study.

CONCLUSIONS

Nanotechnology-based published study formulations discovered it is more optimal for some laboratory tests when expressed as an anticoagulant for the in vivo evaluation of nanoparticle implications on the complement system, and flow cytometer evaluation could be a promising platform approach for use in hemostasis mangers. However, because of the limitations identified in the current study, the results of the systematic review may be estimated. To clarify our outcomes, linearly increasing basic study is needed in the future. One of the most serious issues with both of these novel assays would be a lack of consistency and variation in marker parameters. If we try to describe and select patient groups with different reports focusing on assay factors, the actual increase might not have been large enough here to impair clinical benefit. Several of the novel assays show improvement in terms of increased sensitivity, though their clinical efficacy remains unknown. There are various designs of each strategy, and clinical studies frequently use diverse perspectives, and assay response is heavily dependent on the procedure used. As a result, the findings of the various papers cited in this analysis may be hard to interpret and reproduce. The ongoing efforts at quality control for several of the stronger organizations mean that it can be settled mostly in the nearest future.

Funding: No funding source is reported for this study.

Ethical statement: The author stated that ethical approval is not applicable since it is a review article.

Declaration of interest: No conflict of interest is declared by the author.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the author.

REFERENCES

1. Fadeel, B. Understanding the immunological interactions of engineered nanomaterials: Role of the bio-corona. Wiley Interdiscip Rev Nanomed Nanobiotechnol. 2022;14(6): e1798. https://doi.org/10.1002/wnan.1798 PMid:36416023 PMCid:PMC9787869
2. Skewis LR, Lebedeva T, Papkov V, et al. T2 magnetic resonance: A diagnostic platform for studying integrated hemostasis in whole blood--proof of concept. Clin Chem. 2014; 60(9):1174-82. https://doi.org/10.1373/clinchem.2014.223735 PMid:24958814
3. Warkentin TE. Ischemic limb gangrene with pulses. N Engl J Med. 2015;373(7):642-55. https://doi.org/10.1056/NEJMra1316259 PMid:26267624
4. Warkentin TE, Greinacher A. Laboratory testing for heparin-induced thrombocytopenia. In: Warkentin TE, Greinacher A, editors. Heparin-induced thrombocytopenia. 5th ed. Boca Raton, FL: CRC Press; 2013. p. 272-314. https://doi.org/10.3109/9781841848617
5. Gresele P, Subcommittee on Platelet Physiology of the International Society on Thrombosis and Hemostasis. Diagnosis of inherited platelet function disorders: Guidance from the SSC of the ISTH. J Thromb Haemost. 2015;13(2):314-22. https://doi.org/10.1111/jth.12792 PMid:25403439
6. Ramström AS, Fagerberga IH, Lindahl TL. A flow cytometric assay for the study of dense granule storage and release in human platelets. Platelets. 1999;10(2-3):153-8. https://doi.org/10.1080/09537109909169179 PMid:16801086
7. Manukjan G, Eilenberger J, Andres O, Schambeck C, Eber S, Schulze H. Functional classification of paediatric patients with non-syndromic delta-storage pool deficiency. Hamostaseologie. 2019;39(4): 383-91. https://doi.org/10.1055/s-0038-1675574 PMid:30463093
8. Brunet JG, Iyer JK, Badin MS, et al. Electron microscopy examination of platelet whole mount preparations to quantitate platelet dense granule numbers: Implications for diagnosing suspected platelet function disorders due to dense granule deficiency. Int J Lab Hematol. 2018;40(4): 400-7. https://doi.org/10.1111/ijlh.12801 PMid:29508516
9. William TG, Meera R, Edward PC, et al. A morphometric analysis of platelet dense granules of patients with unexplained bleeding: A new entity of delta-microgranular storage pool deficiency. J Clin Med. 2020;9(6):1734. https://doi.org/10.3390/jcm9061734 PMid:32512725 PMCid:PMC7356033
10. Israels SJ, Kahr WHA, Blanchette VS, Luban NLC, Rivard GE, Rand ML. Platelet disorders in children: A diagnostic approach. Pediatr Blood Cancer. 2011;56(6):975-83. https://doi.org/10.1002/pbc.22988 PMid:21294245
11. Zhang Y, Cui P, Wang Y, Zhang, S. Identification and bioactivity analysis of a newly identified defensin from the oyster magallana gigas. Dev Comp Immunol. 2018;85:177-87. https://doi.org/10.1016/j.dci.2018.04.014 PMid:29733023
12. Hu Z, Yang P, Zhou C, Li S, Hong P. Marine collagen peptides from the skin of Nile tilapia (oreochromis niloticus): Characterization and wound healing evaluation. Mar Drugs. 2017;15(4):102. https://doi.org/10.3390/md15040102 PMid:28358307 PMCid:PMC5408248
13. Ouyang Q, Hou T, Li C, et al. Construction of a composite sponge containing tilapia peptides and chitosan with improved hemostatic performance. Int J Biol Macromol. 2019;139:719-29. https://doi.org/10.1016/j.ijbiomac.2019.07.163 PMid:31356953
14. Wang Q, Li W, He Y, et al. Novel antioxidative peptides from the protein hydrolysate of oysters (crassostrea talienwhanensis). Food Chem. 2014;145:991-6. https://doi.org/10.1016/j.foodchem.2013.08.099 PMid:24128574
15. Zhang Z, Zhou F, Liu X, Zhao M. Particulate nanocomposite from oyster (crassostrea rivularis) hydrolysates via zinc chelation improves zinc solubility and peptide activity. Food Chem. 2018;258:269-77. https://doi.org/10.1016/j.foodchem.2018.03.030 PMid:29655733
16. Xu D, Lin F, Zhu XY, et al. [Immunomodulatory effect of oyster peptide on immunosuppressed mice]. Beijing Da Xue Xue Bao Yi Xue Ban. 2016;48(3):392-7.
17. Asha KK, Remya Kumari KR, Ashok Kumar K, Chatterjee NS, Anandan R, Mathew S. Sequence determination of an antioxidant peptide obtained by enzymatic hydrolysis of oyster *crassostrea madrasensis* (preston). Int J Pept Res Ther. 2016;22:421-33. https://doi.org/10.1007/s10989-016-9521-0

18. Raftery RM, Woods B, Marques ALP, et al. Multifunctional biomaterials from the sea: Assessing the effects of chitosan incorporation into collagen scaffolds on mechanical and biological functionality. Acta Biomater. 2016;43:160-9. https://doi.org/10.1016/j.actbio.2016.07.009 PMid: 27402181
19. Hickman DA, Pawlowski CL, Sekhon UDS, Marks J, Gupta AS. Biomaterials and advanced technologies for hemostatic management of bleeding. Adv Mater. 2018;30(4):10.1002/adma.201700859. https://doi.org/10.1002/adma.201700859 PMid:29164804 PMCid:PMC5831165
20. Kim DK, Jeong J, Shin SD, et al. Association between prehospital field to emergency department delta shock index and in-hospital mortality in patients with torso and extremity trauma: A multinational, observational study. Plos One. 2021;16(10):e0258811. https://doi.org/10.1371/journal.pone.0258811 PMid:34695147 PMCid:PMC8544870
21. Gresele P, Harrison P, Bury L, et al. Diagnosis of suspected inherited platelet function disorders: Results of a worldwide survey. J Thromb Haemost. 2014;12(9):1562-9. https://doi.org/10.1111/jth.12650 PMid:24976115
22. Schafer AI. Bleeding and thrombosis in the myeloproliferative disorders. Blood. 1984;64(1):1-12. https://doi.org/10.1182/blood.V64.1.1.1 PMid:6375757
23. George JN, Caen JP, Nurden AT. Glanzmann's thrombasthenia: The spectrum of clinical disease. Blood. 1990;75(7):1383-95. https://doi.org/10.1182/blood.V75.7.1383.1383 PMid:2180491
24. George JN, Shattil SJ. The clinical importance of acquired abnormalities of platelet function. N Engl J Med. 1991;324(1):27-39. https://doi.org/10.1056/NEJM199101033240106 PMid:1984161
25. Hayward CPM. How I investigate for bleeding disorders. Int J Lab Hematol. 2018;40(Suppl 1):6-14. https://doi.org/10.1111/ijlh.12822 PMid:29741250
26. Hayward CPM, MoffatKA, Brunet J, et al. Update on diagnostic testing for platelet function disorders: What is practical and useful? Int J Lab Hematol. 2019;41 (Suppl 1):26-32. https://doi.org/10.1111/ijlh.12995 PMid:31069975
27. Femia EA, Scavone M, Lecchi A, et al. Effect of platelet count on platelet aggregation measured with impedance aggregometry (multiplate analyzer) and with light transmission aggregometry. J Thromb Haemost. 2013;11(12):2193-6. https://doi.org/10.1111/jth.12432 PMid:24148217
28. Paniccia R, Priora R, Liotta AA, et al. Platelet function tests: A comparative review. Vasc Health Risk Manag. 2015;11:133-48. https://doi.org/10.2147/VHRM.S44469 PMid:25733843 PMCid:PMC4340464
29. Michelson AD. Platelet function testing in cardiovascular diseases. Circulation. 2004;110(19):e489-93. https://doi.org/10.1161/01.CIR.0000147228.29325.F9
30. Christie D, Avari T, Carrington L, et al. Platelet function testing by aggregometry; Approved guideline. H58-A. 2008;28(31):1-45.
31. Hayward CPM, Moffat KA, Raby A, et al. Development of North American consensus guidelines for medical laboratories that perform and interpret platelet function testing using light transmission aggregometry. Am J Clin Pathol. 2010;134(6):955-63. https://doi.org/10.1309/AJCP9V3RRVNZMKDS PMid:21088160
32. Cattaneo M, Cerletti C, Harrison P, et al. Recommendations for the standardization of light transmission aggregometry: A consensus of the working party from the platelet physiology subcommittee of SSC/ISTH. J Thromb Haemost. 2013. https://doi.org/10.1111/jth.12231 PMid: 23574625
33. Shattil SJ, Cunningham M, Hoxie JS. Detection of activated platelets in whole blood using activation-dependent monoclonal antibodies and flow cytometry. Blood. 1987; 70(1):307-15. https://doi.org/10.1182/blood.V70.1.307.307 PMid:3297204
34. Huskens D, Sang Y, Konings J, et al. Standardization and reference ranges for whole blood platelet function measurements using a flow cytometric platelet activation test. PLoS One. 2018;13(2):e0192079. https://doi.org/10.1371/journal.pone.0192079 PMid:29389990 PMCid: PMC5794146
35. van der Vorm LN, Li L, Huskens D, et al. Analytical characterization and reference interval of an enzyme-linked immunosorbent assay for active von Willebrand factor. PLoS One. 2019;14(2):e0211961. https://doi.org/10.1371/journal.pone.0211961 PMid:30759116 PMCid: PMC6373957
36. Ding J, Zhang J, Li J, et al. Electrospun polymer biomaterials. Prog Polym Sci. 2019;90:1-34. https://doi.org/10.1016/j.progpolymsci.2019.01.002
37. Xie X, Chen Y, Wang X, et al. Electrospinning nanofiber scaffolds for soft and hard tissue regeneration. J Mater Sci Technol. 2020;59:243-61. https://doi.org/10.1016/j.jmst.2020.04.037
38. Haider A, Haider S, Kang IK. A comprehensive review summarizing the effect of electrospinning parameters and potential applications of nanofibers in biomedical and biotechnology. Arab J Chem. 2018;11(8):1165-88. https://doi.org/10.1016/j.arabjc.2015.11.015
39. Sergi R, Cannillo V, Boccaccini AR, Liverani L. A new generation of electrospun fibers containing bioactive glass particles for wound healing. Materials (Basel). 2020;13(24): 5651. https://doi.org/10.3390/ma13245651 PMid:33322335 PMCid:PMC7763513
40. Garcia CEG, Bossard F, Rinaudo M. Electrospun biomaterials from chitosan blends applied as scaffold for tissue regeneration. Polymers (Basel). 2021;13(7):1037. https://doi.org/10.3390/polym13071037 PMid:33810406 PMCid:PMC8036406
41. Zanchetta FC, Trinca RB, Gomes Silva JL, et al. Effects of electrospun fibrous membranes of poly-caprolactone and chitosan/poly(ethylene oxide) on mouse acute skin lesions. Polymers (Basel). 2020;12(7):1580. https://doi.org/10.3390/polym12071580 PMid:32708645 PMCid:PMC7408160
42. Heemskerk JWM, Bevers EM, Lindhout T. Platelet activation and blood coagulation. Thromb Haemost. 2002;88(2):186-93. https://doi.org/10.1055/s-0037-1613209 PMid: 12195687
43. Krystin K, Preußе P, Warkentin TE, Trabhardt C, Brandt S, Jensch I, et al. Fibronectin modulates formation of PF4/heparin complexes and is a potential factor for reducing risk of developing HIT. Blood. 2019;133(9):978-89. https://doi.org/10.1182/blood-2018-05-850370 PMid: 30573633

44. Adam C, Husseinzadeh H, Lebedeva T, Marturano JE, Massefski W, Lowery TJ, et al. Rapid evaluation of platelet function with T2 magnetic resonance. Am J Clin Pathol. 2016;146(6):681-93. https://doi.org/10.1093/ajcp/aqw189 PMid:28028118 PMCid:PMC5225753
45. Volodymy D., Sulaieva O, Pernakov M, Korniienko V, Husak Y, Yanovska A, et al. Hemostatic and tissue regeneration performance of novel electrospun chitosan-based materials. Biomedicines. 2021;9(6):588. https://doi.org/10.3390/biomedicines9060588 PMid:34064090 PMCid:PMC8224387
46. Asten Van I, Blaauwgeers M, Granneman L, Heijnen HFG, Kruip MJHA, Beckers EAM, et al. Flow cytometric mepacrine fluorescence can be used for the exclusion of platelet dense granule deficiency. J Thromb Haemost. 2020;18(3):706-13. https://doi.org/10.1111/jth.14698 PMid:31815339 PMCid:PMC7065135
47. Zhang D, Hu Z, Zhang L, Lu S, Liang F, Li S. Chitosan-based thermo-sensitive hydrogel loading oyster peptides for hemostasis application. Materials. 2020 9;13(21):5038. https://doi.org/10.3390/ma13215038 PMid:33182319 PMCid:PMC7664874
48. Kagkelaris K, Panayiotakopoulos G, Georgakopoulos CD. Nanotechnology-based formulations to amplify intraocular bioavailability. Ther Adv Ophthalmol. 2022;14:25158414221112356. https://doi.org/10.1177/25158414221112356 PMid:35873277 PMCid:PMC9301101
49. Huskens D, Li L, Florin L, de Kesel P, de Laat B, Roest M, Devreese KMJ. Flow cytometric analysis of platelet function to improve the recognition of thrombocytopathy. Thrombosis Res, 2020;194:183-9. https://doi.org/10.1016/j.thromres.2020.06.037
50. Ranucci M, Laddomada T, Ranucci M, Baryshnikova E. Blood viscosity during coagulation at different shear rates. Physiol Rep. 2014;2(7):e12065. https://doi.org/10.14814/phy2.12065 PMid:24994896 PMCid:PMC4187573
51. Bock PE, Srinivasan K, Shore JD. Activation of intrinsic blood coagulation by ellagic acid: Insoluble ellagic acid-metal ion complexes are the activating species. Biochemistry. 1981;20(25):7258-66. https://doi.org/10.1021/bi00528a032 PMid:6797471
52. Miyazawa K, Fogelson AL, Leiderman K. Inhibition of platelet-surface-bound proteins during coagulation under flow I: TFPI. Biophys J. 2023;3;122(1):99-113. https://doi.org/10.1016/j.bpj.2022.11.023 PMid:36403087
53. Nielsen VG, Geary BT, Baird MS. Evaluation of the contribution of platelets to clot strength by thromboelastography in rabbits: The role of tissue factor and cytochalasin D. AnesthAnalg. 2000;91(1):35-9. https://doi.org/10.1097/00000539-200007000-00007 PMid:10866883
54. Ganter MT, Hofer CK. Coagulation monitoring: Current techniques and clinical use of viscoelastic point-of-care coagulation devices. Anest Analg. 2008;106(5):1366-75. https://doi.org/10.1213/ane.0b013e318168b367 PMid:18420846
55. Harris LF, Castro-López V, Killard AJ. Coagulation monitoring devices: Past, present, and future at the point of care. TrAC Trends Analyt Chem. 2013;50:85-95. https://doi.org/10.1016/j.trac.2013.05.009
56. Jones CG, Pechauer SM, Curtis BR, Bougie DW, Aster RH, Padmanabhan A. Normal plasma IgG inhibits HIT antibody-mediated platelet activation: Implications for therapeutic plasma exchange. Blood. 2018;131(6):703-6. https://doi.org/10.1182/blood-2017-08-803031 PMid:29259003 PMCid:PMC5805490
57. Selleng S, Selleng K, Wollert HG, et al. Heparin-induced thrombocytopenia in patients requiring prolonged intensive care unit treatment after cardiopulmonary bypass. J Thromb Haemost. 2008;6(3):428-35. https://doi.org/10.1111/j.1538-7836.2007.02870.x PMid:18088340
58. Mumford AD, Frelinger A, Gachet C, et al. A review of platelet secretion assays for the diagnosis of inherited platelet secretion disorders. Thromb Haemost. 2015;113:1-12. https://doi.org/10.1160/TH14-11-0999 PMid:25879272
59. Moenen F, Nelemans PJ, Schols SEM, et al. The diagnostic accuracy of bleeding assessment tools for the identification of patients with mild bleeding disorders: A systematic review. Haemophilia. 2018;24(4):525-35. https://doi.org/10.1111/hae.13486 PMid:29873431
60. Bian J, Bao L, Gao X, et al. Bacteria-engineered porous sponge for hemostasis and vascularization. J Nanobiotechnol. 2022;20:47. https://doi.org/10.1186/s12951-022-01254-7 PMid:35062972 PMCid:PMC8780714
61. Neun BW, Ilinskaya AN, Dobrovolskaia MA. Analysis of complement activation by nanoparticles. Methods Mol Biol. 2018;1682:149-60. https://doi.org/10.1007/978-1-4939-7352-1_13 PMid:29039100
62. Kapur NK, Shenoy C, Yunis AA, et al. Distinct effects of unfractionated heparin versus bivalirudin on circulating angiogenic peptides. PLoS One. 2012;7(4):e34344. https://doi.org/10.1371/journal.pone.0034344 PMid:22509290 PMCid:PMC3324508