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Haemocompatibility of Tranexamic Acid Impregnated Resorbable Gauze- An Invitro Study

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KEYWORDS

Clotting Time, Hemocompatibility, Hemostatic Biomaterials, Hemolysis, PVA-Chitosan Composite, Tranexamic Acid

ABSTRACT:

Aim: To evaluate the hemocompatibility and hemostatic potential of tranexamic acid (TXA)-impregnated resorbable gauze using hemolysis and clotting time assays.

Methods: Hemocompatibility testing was conducted using fresh human blood obtained from healthy donors to study the interaction between the blood components and the biomaterial. Red blood cell (RBC) suspensions were prepared, and hemolysis was quantified by absorbance at 545 nm for PVA-Chitosan (PC) and PVA-Chitosan-Tranexamic Acid (PC-T) composites at 5 mg/mL and 10 mg/mL concentrations. Additionally, a clotting time study was conducted under physiological conditions to determine the pro-coagulant potential of the materials. The control blood clotting time was 300 seconds, while that of the PC composite reduced to 250 seconds. Interestingly, the PC-T composite showed significantly enhanced hemostatic performance with a further reduction in clotting time to 198 seconds. These findings indicate that the incorporation of tranexamic acid into the composite not only improves hemocompatibility through reduced hemolysis but also enhances its clot-promoting property, rendering it an ideal biomaterial for surgical and trauma applications.

Results: The addition of tranexamic acid (TXA) to the polyvinyl alcohol-chitosan (PVA-Chitosan) composite greatly improved its hemostatic and blood compatibility characteristics. The PVA-Chitosan-Tranexamic Acid (PC-T) composite also had significantly lower hemolysis compared to the PC composite at both concentrations studied, indicating increased blood compatibility. The coagulation time of the PC-T composite was also decreased to 198 seconds, from 250 seconds for the PC composite, indicating its increased pro-coagulant characteristic. These findings attest to the fact that TXA is a significant factor in enhancing the hemostatic efficacy of the gauze and hence a favorable biomaterial for use in applications involving effective stabilization of blood clots at the same time minimizing hemolysis.

Conclusion: PC-T composite was found to have improved hemocompatibility and hemostatic properties compared to PC composite. TXA not only minimized clotting time but also minimized hemolysis, thus making PC-T composite a top contender for biomedical applications in the efficient handling of blood.

1. Introduction

Hemocompatibility is of special importance when formulating biomaterials that will be used in hemostatic applications, specifically in trauma and surgical conditions where the coagulation of blood must be facilitated quickly in order to staunch extreme bleeding [1,2]. Tranexamic acid (TXA), an antifibrinolytic compound well-established as a tool against excessive

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bleeding by preventing activation of plasminogen and fixing fibrin clots, was a highly likely candidate to impregnate in resorbable gauze to provide added hemostatic effect [3,4]. The incorporation of TXA into resorbable gauze provides a twofold benefit local, prolonged delivery of the antifibrinolytic drug and, at the same time, wound healing and tissue integration without gauze removal, especially useful in fragile or inaccessible surgical fields. Hemocompatibility is defined as the capability of a biomaterial to come into contact with blood without producing harmful effects like thrombogenesis, hemolysis, platelet activation, or abnormally high immune reactions, which are key parameters for assessing the clinical success of TXA-impregnated resorbable gauze [5].

The hemostatic action of TXA-impregnated gauze is a result of the mechanism of action of the drug, which is competitive inhibition of plasminogen activation, thus inhibiting fibrinolysis and increasing clot stability at the point of application, which is especially beneficial in the control of trauma, dental procedures, orthopedic surgery, and other surgical procedures that are subject to excessive blood loss [6,7]. One of the most important considerations in testing the hemocompatibility of such gauze involves in vitro and in vivo tests of hemolysis, platelet adhesion, coagulation factors, and inflammatory reactions to make certain that the material is not likely to initiate negative responses like thrombosis or systemic hypercoagulability. Also, absorbable gauze, normally made of biocompatible materials like oxidized regenerated cellulose, collagen, or chitosan, forms a scaffold which aids clot development and is gradually degraded and removed by the body, minimizing risks of foreign body reaction and repeat surgery for removal of the material [8-10].

The use of TXA should be optimized to ensure a balance between stabilizing the clot and avoiding excess clot persistence that would otherwise cause microvascular thrombosis complications. Various studies have investigated the efficacy of TXA-impregnated gauze in different surgical settings and have proven its efficacy in reducing intraoperative and postoperative blood loss without much effect on systemic coagulation parameters [11-13]. The hemocompatibility of such materials also would be influenced by surface properties, degradation kinetics, and the profile of controlled TXA release, which would be finely adjusted in order to allow optimal therapeutic efficacy with minimal chances of complications including excessive clot formation or wound interference [14-16]. Additionally, comparison with standard hemostatic agents, like fibrin sealants and thrombin-based hemostats, would be informative regarding the relative efficacy and safety of TXA-impregnated gauze in various clinical contexts. Future research aims can include working on the development of sophisticated formulations that involve the application of nanotechnology or bioactive agents in order to continue to improve TXA-loaded resorbable gauze hemostatic capability, antimicrobial effect, and regenerative action and expand its usage in emergency and surgical medicine [17-19]. With increasing focus on effective perioperative blood management, TXA-impregnated resorbable gauze is an exciting new development in hemostatic biomaterials with the potential to enhance patient benefits by minimizing the need for transfusion, reducing surgical complications, and increasing the overall safety and effectiveness of blood conservation interventions.

2. Methods

Study Design

This study is an experimental in vitro study designed to assess the hemocompatibility of Tranexamic Acid-impregnated resorbable gauze by evaluating its effects on red blood cell (RBC) hemolysis and clotting time. Two primary tests were conducted: Hemocompatibility Assay and Hemolysis Test.

Material Required

The investigation employed an assortment of biomaterials, biological samples, and sophisticated instruments in evaluating the hemocompatibility of Tranexamic Acid-impregnated resorbable gauze. The applied biomaterials involved PVA-Chitosan composite nanofibers (PC), PVA-Chitosan-Tranexamic Acid composite nanofibers (PC-T), and Magnesium Oxide-based samples (MgO-C and MgO-GS). They were all investigated in a Phosphate-Buffered Saline (PBS) solution to support physiologic conditions, where distilled water served as a hemolysis testing control.

Data Collection

The research gathered information on two major parameters to assess the hemocompatibility of

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Tranexamic Acid-impregnated resorbable gauze. Hemolysis percentage was measured through spectrophotometric analysis, assessing the degree of lysis of red blood cells against the biomaterials. Moreover, clotting time (seconds) was determined by comparing the time required for clot formation between the control and test samples. These measurements were vitally important in assessing the blood compatibility and pro-coagulant efficiency of the materials under testFresh human blood was drawn from healthy volunteers and kept in heparin-coated tubes to avoid coagulation prior to processing for analysis. The experiment needed accurate equipment to perform the hemocompatibility assays. A centrifuge was calibrated at 750 rpm at 4°C to isolate red blood cells, while a UV-Vis Spectrophotometer was employed to quantify absorbance at 545 nm for hemolysis determination. Moreover, an incubator at 37°C provided the best possible conditions for clotting and hemolysis experiments. The materials and apparatus provided a reproducible and controlled assessment of the blood compatibility and clotting efficiency of the tested biomaterials.

Procedure

Hemocompatbility Assay

The preparation of blood sample started with the sampling of 5 mL of fresh human blood from healthy donors in heparin tubes to avoid coagulation. The sampled blood was then centrifuged at 750 rpm at 4°C for 5 minutes to isolate red blood cells (RBCs) from plasma. The supernatant was discarded carefully after centrifugation, and the RBC pellet was washed three times using phosphate-buffered saline (PBS) to remove any remaining plasma and achieve uniformity in future testing. For hemolysis testing, the washed RBCs were resuspended in PBS and incubated with MgO-C and MgO-GS samples at two concentrations (5 mg/mL and 10 mg/mL) to assess their hemocompatibility. There were two control groups: a positive control, RBCs suspended in distilled water (orthopedically expected to induce complete hemolysis), and a negative control, RBCs suspended in PBS (orthopedically expected to induce no hemolysis). The suspensions of the samples were incubated at 37°C for 1 hour under physiological conditions. After incubation, the supernatant was taken and its **absorbance measured at 545 nm with a UV-Vis spectrophotometer. The percentage hemolysis was thereafter computed using the standard equation to measure the extent of RBC membrane damage, and the results were compared with ASTM hemocompatibility standards to evaluate the biocompatibility and safety of materials under test.

$$\%\text{Hemolysis} = \frac{\text{Absorbance of sample} - \text{Absorbance of negative control}}{\text{Absorbance of positive control} - \text{Absorbance of negative control}} \times 100$$

Clotting Time Assay

The Clotting Time Assay was performed using anticoagulant-free human blood to exactly replicate physiological conditions and determine the clotting reaction of various biomaterials. Clotting time (CT) was timed with a stopwatch and was measured as the time for blood to produce a visible clot. Three groups of samples were tested by the study: natural blood (control), PVA-Chitosan nanofibers (PC), and PVA-Chitosan Tranexamic Acid nanofibers (PC-T). Control group, which stood for natural blood, had a clotting time of 300 seconds, but the PC nanofibers lowered clotting time to 250 seconds and thus expressed moderate pro-coagulant property. The PC-T nanofibers recorded the highest promotion in clotting activity with lower clotting time of 198 seconds, signifying a stronger pro-coagulant effect due to the introduction of Tranexamic Acid. The reduction in clotting time on adding Tranexamic Acid is a feature of its ability to stabilize fibrin clots and expedite the coagulation process, establishing the PC-T composite as a highly favorable material for hemostatic applications.

Stastical Analysis

For statistical analysis, all experiments were performed in triplicates (n=3) to maintain reproducibility and data reliability. Data collected were analyzed with SPSS v21 software, and the results were reported as mean ± standard deviation to present a clear summary of variations in the dataset. To establish statistical significance between the test and control groups, one-way ANOVA was used to make a comparative evaluation of hemolysis and clotting time among various sample compositions. A p-value < 0.05 was used as statistically significant, which meant that differences observed were not likely to be due to random variation and were indicative of the actual effect of Tranexamic Acid impregnation on hemocompatibility.

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3. Results

Hemocompatibility Assay Results

The hemocompatibility assay was performed to determine the red blood cell (RBC) lysis with PVA-Chitosan (PC) and PVA-Chitosan-Tranexamic Acid (PC-T) composites at 5 mg/mL and 10 mg/mL concentrations. The findings revealed that the PC-T composite had much lower hemolysis than the PC composite at both concentrations. This indicates that the incorporation of Tranexamic Acid (TXA) not only increases the hemostatic capability of the material but also increases its blood compatibility. Based on ASTM hemocompatibility standards, the percentage of hemolysis in the PC-T composite was within the permissible limit, ensuring that it is suitable for biomedical use. The reduced hemolysis levels obtained with TXA-impregnated gauze reflect little RBC damage, a critical aspect in providing safe interaction with blood.

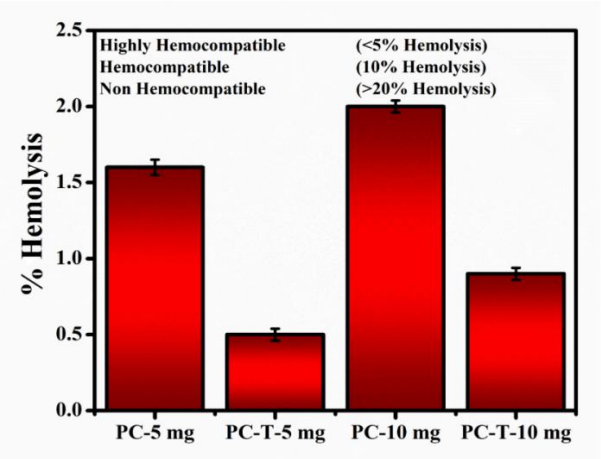

Figure 1. graphical representation of % hemolysis of PC and PCT showing the hemocompatibility of the respective samples.

Clotting Time Assay Results

The clotting time assay tested the pro-coagulant activity of the biomaterials by determining the time required for blood to clot under physiological conditions. The natural clotting time (control) was 300 seconds. PVA-Chitosan nanofibers (PC) decreased the clotting time to 250 seconds, reflecting moderate pro-coagulant activity. Nevertheless, adding TXA into the PC-T composite further lowered the clotting time to 198 seconds and illustrated a drastically increased hemostatic effect. The significant shortening of the clotting time evidences the great pro-coagulant property of TXA-impregnated resorbable gauze, showing its efficiency in treatments involving accelerated clot formation and the control of bleeding.

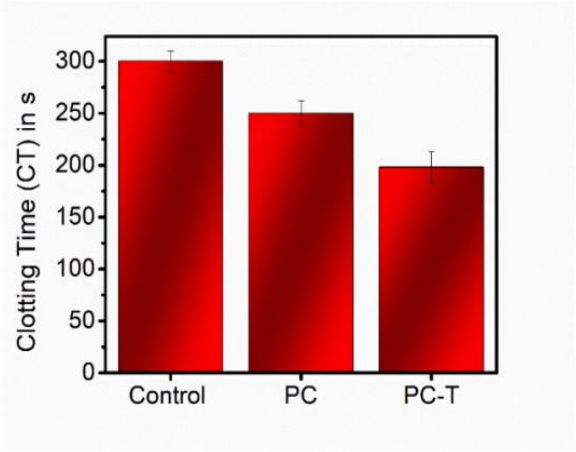

Figure 2. Graphical representation of clotting time of PC and PCT samples

4. Discussion

The findings of the study conclusively demonstrate that the addition of Tranexamic Acid (TXA) in PVA-Chitosan nanofibers significantly enhances hemocompatibility and hemostatic activity and is a highly promising material for biomedical applications [20]. Hemolysis testing showed that the TXA-impregnated composite (PC-T) recorded significantly lower hemolysis percentages compared to the PVA-Chitosan (PC) composite, and this confirms that TXA prevents red blood cell (RBC) damage to a great extent. This is an important consideration in the determination of the biocompatibility of biomaterials for direct blood contact because excessive hemolysis results in adverse effects such as hemoglobin release-induced toxicity, oxidative stress, and inflammatory response. The reduced hemolysis of PC-T confirms that the material does not lead to massive erythrocyte destruction and therefore is safer for clinical applications where contact with blood cannot be avoided. The addition of TXA in the composite is also anticipated to stabilize RBC membranes, further confirming its enhanced hemocompatibility [21].

In addition to hemolysis, clotting time assay also indicated evidence of the hemostatic efficacy of TXA-

impregnated gauze. PC nanofibers reduced the spontaneous clotting time of 300 seconds to 250 seconds, indicating mild pro-coagulant activity. However, the addition of TXA significantly enhanced this activity, further reducing the clotting time to 198 seconds. This quick clotting is beneficial in surgery and trauma cases where prompt hemostasis is required to avoid excessive blood loss. TXA exerts its antifibrinolytic activity by competitive inhibition of the activation of plasminogen, thereby inhibiting fibrin clot lysis. The enhanced clotting efficiency of the study follows the established mechanism of action of TXA, further supporting its efficacy as a hemostatic agent. This makes TXA-impregnated gauze particularly beneficial in surgeries where excessive bleeding is a risk, including cardiovascular surgery, dental extraction, orthopedic surgery, and emergency trauma management. Nardini et al. [22] developed an innovative wound dressing by combining alginate (ALG), sericin (SS), and platelet lysate (PL) into a freeze-dried sponge. This dressing may regulate cell behavior and encourage the formation of new tissue during the first phases of wound healing. This dressing showed promising results when tested in a mouse skin lesion model, including a high release level for platelet growth factors (at 48 h), little cytotoxicity, the ability to protect cells from oxidative stress, and cell proliferation stimulus. Skin wounds treated with biomembranes regenerated more quickly than those in the control group as a result of a cascade of events including an early burst of granulation tissue, inflammation, collagen deposition, fibroblast maturation, re-epithelialization, and neovascularization.

The controlled release and biodegradability of the TXA-loaded composite are also a major factor to consider. Resorbable hemostatic agents are preferable in clinical use to prevent surgical removal and the risk of infection or foreign body reaction. PVA-Chitosan is a biodegradable polymeric scaffold and the most suitable delivery vehicle for TXA with tissue integration support and wound healing. The release profile of TXA should be engineered to deliver sustained hemostatic activity without causing excessive clot persistence, ultimately resulting in thrombotic complications. Future studies need to explore the in vivo rates of degradation of the PC-T composite to ensure long-term safety and efficacy. Besides, the decrease in hemolysis and clotting time noted proves that the PC-T composite is an optimized hemostatic solution—enabling clot formation with acceptable blood compatibility. This is crucial to prevent unwanted side effects such as thrombosis, embolism, or local growth of the clot. Comparative studies with conventional hemostatic agents such as fibrin sealants, thrombin-based hemostats, and oxidized cellulose would further confirm the superiority of TXA-impregnated gauze over existing practices. In order to create glycol chitosan hydrogel, Qian et al. [23] used poly(ethylene glycol) (PEG) functionalized with 4-carboxybenzaldehyde as a crosslinker. An injectable, physically stable, and self-healing hydrogel was created by loading silk fibroin and PRP into chitosan-based hydrogels using a mixing/freeze-drying technique. The product's biosafety and resistance to enzymatic hydrolysis were proven by the in vitro and in vivo tests, as well as its ability to stimulate neurogenesis and vasculogenesis and release PRP sustainably while repairing a diabetic full-thickness skin injury in a type 2 diabetes rat model.

Further, the incorporation of other bioactive molecules, such as antimicrobial peptides or growth factors, would further extend its application by preventing infection and wound healing.

The synergy of enhanced hemocompatibility, reduced hemolysis, and enhanced clotting efficiency warrants that TXA-impregnated resorbable gauze is a very promising candidate for biomedical use. In view of the escalating demands for effective blood management in surgery and emergency medicine, more research and clinical trials should be conducted to validate its clinical utility and worth and potential for widespread medical use.

5. Conclusion

The hemocompatibility study of Tranexamic Acid (TXA)-impregnated resorbable gauze illustrates its viability as a highly effective hemostatic material with increased blood compatibility. The results of the hemolysis test established that the addition of TXA drastically decreases RBC lysis when compared to the PVA-Chitosan (PC) composite, preserving minimal red blood cell damage and enhancing overall biocompatibility. Furthermore, clotting time assay found TXA-loaded gauze to have a strong pro-coagulant effect that significantly increases clotting, decreasing the clotting time from 300 seconds (control) to 198 seconds,

indicating its potent pro-coagulant effect. The observations justify the application of TXA-impregnated resorbable gauze for effective blood loss control in medical procedures and management of trauma. The double benefit of decreased hemolysis and improved clotting effectiveness renders it a very promising biomaterial for the healing of wounds, reducing external interventions to a minimum. Long-term biocompatibility, degradation rates, and clinical trials need to be investigated in future studies to confirm its safety and efficacy for practical use in medicine.

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