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Development of a cost-effective plasma thawer for blood transfusion in low-resource settings

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Abstract:

Plasma thawers are vital in healthcare, ensuring the safe thawing of frozen plasma for life-saving transfusions. To address challenges such as specialized operator training and high initial costs in low-resource settings, we developed a cost-effective and efficient plasma thawer in Pakistan. The device consisted of two compartments: one dedicated to thawing plasma and equipped with a water-filled heater, a continuous temperature sensor, and an agitating frame for plasma bags, and the other housing the control box. Optimized thawing conditions were defined. The temperature regulation and control of motors were coordinated through an Arduino microcontroller and relays allowing users to set temperature limits through push buttons. We report that the prototype maintained a consistent water temperature between 37-40°C, with a minimal deviation of ±1°C. We observed an average thawing time of 12, 14, and 16 minutes for one, two, and three plasma bags respectively. Efficiency metrics revealed an 80% thawing efficiency compared to standardized methods, with temperature control consistency ranging from 95% to 99% depending on the number of bags. Completion signal reliability reached 94.6%, effectively preventing uncontrolled thawing. Plasma samples were free of solid or gelatinous particles, demonstrating no protein denaturation or overheating. The prototype was 10-fold more cost-effective than commercially available alternatives. We demonstrate that plasma can be thawed using our prototype without any negative influence on the plasma quality, presupposing that optimized settings defined for this plasma product are used. We plan to assess plasma coagulation, inhibition activity, and hemostatic potency to further define device functionality.

Keywords: *Plasma thawer; Plasma Thawing; Low-cost Healthcare Devices; Resource-limited Settings; Temperature Control System.*

1. Introduction

Fluid resuscitation is vital for maximizing survivability following blood loss [1]. Previous studies have reported that resuscitation with blood products is superior to crystalloid solutions [2]. Refrigerated plasma and red blood cell (RBC) concentrates are

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commonly used blood products in rural or low-resource settings [3]. Plasma contains important clotting factors and is indicated for complex coagulopathy associated with manifest or imminent bleeding in massive transfusion, for the reversal of warfarin in the presence of active bleeding, and for congenital or acquired factor deficiency with no alternative therapy [4].

Fresh frozen plasma is stored at -30ºC and requires on-demand thawing at a temperature range of 30-37ºC [5]. The activity of clotting factors like factor V and factor VIII declines gradually once thawed. The thawing period must not be excessively long or rapid as it can damage coagulation enzyme function. Thus, plasma thawer devices ensure an efficient and regulated thawing process while preserving the biological integrity and therapeutic effectiveness of the blood product [5]. There has been an increase in the usage of plasma thawing systems worldwide, due to the rising incidence of hematological diseases, rapid technological advancements, and a greater awareness of the benefits of plasma therapy [6]. Previously, it has been demonstrated that plasma samples subjected to up to 10 freeze-thaw cycles with quick freezing and thawing exhibited remarkably stable metabolite levels [7].

Conventional water baths remain comparable to novel techniques such as dry heat, microwave, and radiofrequency in terms of thawing performance [8]. In addition, automated and closed-system thawers provide a sterile environment and reduce the danger of contamination. However, there are still certain drawbacks to frozen plasma thawing such as the requirement for operators to have specialized training and high initial costs which may be difficult to achieve in Low-and Middle-Income Countries (LMICs) such as Pakistan.

In this study, we aim to develop a cost-effective, and portable device that can thaw frozen plasma units while maintaining the quality of the plasma, specifically tailored for local manufacturing and resource availability in Pakistan.

2. Methodology

2.1. Working principle

The plasma thawer utilized a water bath to maintain plasma units at optimal thawing temperatures, typically between 30 and 37ºC. Key components, such as a heater, relays, a gear motor, a temperature sensor, push buttons, and an Arduino microcontroller, worked together to raise the water temperature in a controlled environment.

2.2. Plasma bag preparation

We obtained fifteen fresh frozen plasma (FFP) bags from Dow Laboratory, Karachi. Pakistan. The samples were selected randomly, and all procedures were conducted by a single phlebotomist and a dedicated technician team for coagulation analysis. We included samples with blood group O donations during the study period, donors aged 18-30 years, FFPs prepared within one hour of blood collection, and coagulation assays conducted within 15 minutes of product preparation. Our exclusion criteria comprised donations from outdoor camps, bags subjected to prolonged thawing, bags damaged during the procedure, and samples with failed results in coagulation analyzer tests. The FFP collection and preparation process involved collecting 450 mL of blood from each donor, centrifuging the blood using a Cryofuge 6000i, extracting the plasma with a Fenwall system, immediately assessing the plasma for Prothrombin Time (PT), activated Partial Thromboplastin Time (aPTT), fibrinogen levels, and Factor VIII, snap-freezing the plasma at -80°C, and finally shifting the snap-frozen plasma to a -30°C freezer within 24 hours after infection screening.

2.3. Designed system

We constructed the prototype using locally available components, each playing a crucial role in the system's functionality (fig 1). A metallic tank provided a structural foundation. It comprised two compartments – one equipped with racks for immersing plasma bags in water and the other

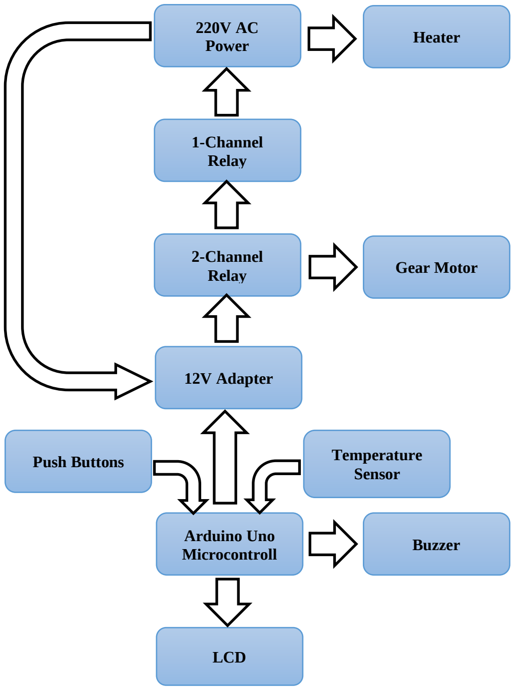

Fig 1. Block diagram of the plasma thawer

served as the control box housing the motor and circuitry. A powerful 1500-watt, 6.8 Amp heater elevated the water temperature within the tank. The system integrated two types of relay: a 12V 1-channel relay to control the heater, and a 2-channel relay module connected to the Arduino microcontroller, responsible for managing both the 1-channel relay and a 24V gear motor.

The motor provided linear motion to produce to-and-fro movements of the racks that support plasma bags. We used a DS18B20 sensor for temperature measurement. Push buttons were implemented for setting cycle times and initiating operations and a buzzer signaled the completion of set time. The Arduino UNO was the central processing unit, interfacing with various components to collect and process electrical signals.

Electrical connectivity was established using a veroboard, with jumper wires with connector pins at either end. Fig 2 describes the circuit diagram of the prototype. Power was supplied to the relays, Arduino microcontroller, and motor through an adapter providing 12V. The system's output, including temperature and time, was displayed on a 16 × 2 liquid crystal display (LCD).

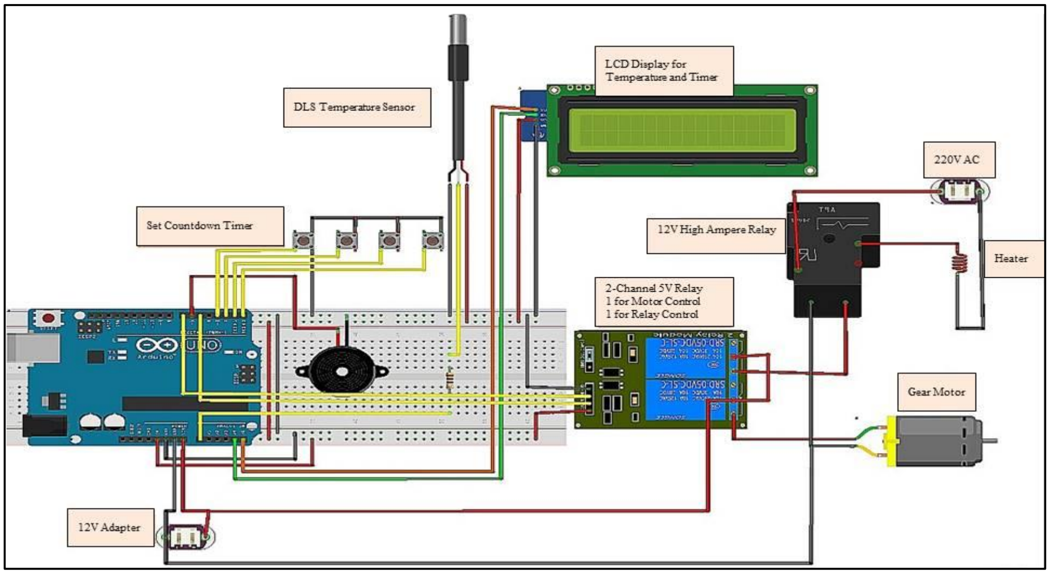

Fig 2. Circuit diagram of the plasma thawer

2.4 Components required

A list of different components used to construct the plasma thawer, with their detailed specifications are:

1. **Heater:** Model ID: Auto Kettle Element Water Boiler Water Heater Copper Element Immersion Rod Thermal Auto Clave (1500w).
2. **1-Channel Relay:** FC-65 12V 30-AMP 1-Channel Relay Module SLA-12VDC-SL-C
3. **2-Channel Relay**: Brand : Generic Model : 5V 2 Channel
4. **Gear Motor:** IG42 24VDC 340 RPM Gear Motor with Encoder
5. **Temperature sensor:** ds18b20 temperature sensor
6. **Push Buttons:** Product Name : Tact Switch
   Part Number : KG-2
7. **Arduino Uno Microcontroller**: Microcontroller : ATmega328P Arduino Uno Rev 3
8. **Adapter**: 12V 4A 48W AC Adapter/Power Supply/Charger+US Power Cord for LCD Monitor UpBright NEW Global AC DC Adapter For 12V 4A 48W 5.5mm x 2.5mm Connector Tip LCD Monitor 12VDC 12 Volts 4 Amps 4.0A - 4.16A 48 - 50W Switching Power Supply Cord Cable Charger Mains PSU
9. **Buzzer:** HXD buzzer YMD-12095 Model Number : buzzer Brand Name : XIN NUO QI
10. **LCD Display:** Controller HD44780 or equivalent controller 16×2 LCD Display 1602 Character Display for Arduino – Blue

The heating process and agitation were initiated after the user inputs the operating time, mode, and temperature range on the control panel. If the temperature decreased below a specified lower limit, a network of relays enables the flow of 220 volts to the heater. If the temperature surpassed the upper limit, the Arduino signals discontinue the power supply, ensuring the temperature stays within the user-defined limits. An Arduino-controlled relay allowed the continuous flow of 12 volts to the motors for the agitation of plasma bags until the cycle stopped. The time required for complete thawing under preset temperature and time parameters was meticulously recorded for each unit. The samples were visually checked for the completeness of thawing without any manipulation in the process. The completion of each cycle was indicated by the device automatically shutting off and emitting an alarm to prevent uncontrolled thawing. We measured the thawing time for each cycle for 1, 2, and 3 bags. We collected data on temperature, user inputs, cycle times, completion signals, and visual inspection. All reported results were expressed as mean ± standard deviation.

We verified the temperature sensor accuracy against a calibrated thermometer and confirmed the time synchronization for accurate recording. We double-checked cycle times by the engineers, and completion signals were validated for reliability. We assessed the plasma thawer's performance using efficiency metrics including thawing time, temperature control, completion signal reliability, user input accuracy, and visual inspection results.

2.5 Parameter description

Thawing time efficiency was determined by calculating the average thawing time and comparing it to standardized methods [5] which is calculated as follows:

Thawing Time Efficiency:

$$= 1 - \frac{Prototype\ Thawing\ Time}{Standard\ thawing\ time} X100$$

Temperature control efficiency evaluated the device's ability to consistently maintain the desired temperature range as shown in the formula below.

Temperature Control Efficiency

$$= \frac{Desired\ Temperature\ Range\ Maintained}{Total\ time} X100$$

Completion signal reliability was assessed by calculating the percentage of cycles where uncontrolled thawing is prevented. It is quantitatively measured through the use of the given formula:

Reliability (Completion Signal Reliability)

$$= \frac{Number\ of\ Successful\ Cycles}{Total\ cycles\ conducted} X100$$

Table 1 Validation and performance metrics of the prototype

Validation Aspect	**Deviation/Percentage**
Temperature Sensor Accuracy	±1.0°C
Time Synchronization	±3 seconds
Cycle Times Deviation	±2 seconds
Completion Signal Reliability	94.6%
Efficiency Metrics	
Thawing Time Efficiency	80%
Temperature Control Efficiency	97%
User Input Accuracy	90.6%
Visual Inspection Results	92.6%

User input accuracy examined adherence to specified parameters, and visual inspection results were correlated with device signals. Formula for this is given below:

Accuracy (User Input Accuracy)

$$= \frac{Correctly\ Adhered\ Parameters}{Total\ specified\ parameters} X100$$

We reviewed the recorded data to identify inconsistencies, ensuring values were within expected ranges. Cost-effectiveness was determined by calculating the total expenses and comparing them to industry benchmarks.

3. Results and discussion

We describe the performance of the functional prototype in terms of the thawing time, temperature control, and completion signal reliability (Table 1). Among all the completed cycles, we observed that the temperature sensor exhibited a deviation of ±1.0 °C, time synchronization was well-maintained, with a deviation of ±3 seconds, and cycle times showed a deviation of ±2 seconds. The device thawing rate was 80% similar to standard conditions indicating that the system was able to consistently maintain the desired temperature range during the thawing process. In addition, the device was 94.6% effective in signaling the completion of each thawing cycle and preventing uncontrolled thawing. The thawer accurately adhered to specified parameters 90.6% of the time, including operating time, mode, and temperature range. There was 92.6% concordance between the device's signals and the observed completeness of thawing during visual inspections, reducing the need for manual intervention and enhancing overall operational efficiency.

The functional prototype showcased consistent performance within specified parameters. The samples were clear of solid and gelatinous particles, indicating no protein denaturation or overheating. The device was ten times more cost-effective compared to

Table 2 Comparative analysis of our prototype with previous studies

Study/Device	Thawing Time (1 Bag)	Temperature Deviation	Completion Signal Reliability	Cost	Special Notes
Current Study (Shahid et al., 2024)	12 minutes	±1°C	94.6%	PKR 8,000 (~$25)	Locally manufactured; cost-effective solution for low-resource settings.
Pinki et al., 2017 Dry Heat Thawing)[8]	15 minutes	±2°C	92%	N/A	Dry heat; lower contamination risk; slightly longer thawing time.
Tanigawa et al.,2013(Microwave Thawing)[11]	5 minutes	±1.5°C	90%	High (>$5,000)	Rapid thawing; uneven heating and risk of protein denaturation.
Casewell et al., 1981 (Water Bath) [10]	10-12 minutes	±1°C	90%	~$200	Widely used; risk of bacterial contamination in water.
Keller-Stanislawski et al., 2009 (Sterile Bath) [9]	10 minutes	±0.5°C	98%	N/A	High precision; used in high-resource clinical environments.

commercially available alternatives. Previous studies have shown instances of mixed bacterial growth, predominantly featuring Pseudomonas isolates, in samples obtained from water baths [9, 10]. However, we did not collect data on the frequency of bacterial contamination in our water bath technique. Previous studies have also shown that microwaves were more effective in shortening time, maintaining safety, and the clotting factor activity in thawed FFP than in water baths [11]. Thus, future analyses are imperative to comprehensively understand the denaturation in plasma proteins, especially heat-labile clotting factors, during the thawing process as compared to other techniques.

Table 2 shows a comparison of our prototype with previously published studies. With a thawing time of 12 minutes, our device was quicker than the dry heat thawing method [8], which took 15 minutes, but slower than the microwave thawing method [11] at 5 minutes. Our temperature deviation of ±1°C was slightly higher than the more precise sterile bath [9] and plasma thawer [13], both at ±0.5°C. The reliability of our device (94.6%) was lower than the sterile bath plasma thawer (98%) but still higher compared to other methods like microwave thawing (90%).

We also systematically compared the thawing characteristics observed while using one, two, and three bags to discern variations in the performance metrics (Table 3). The average thawing time for operational efficiency increased gradually from 12 minutes for one bag to 16 minutes for three bags respectively. Thawing efficiency compared to standard conditions decreased from 86.6% for one bag to 73.3% for three bags. Temperature control, a critical aspect for preserving plasma quality, exhibited a deviation across all scenarios, with ±0.1°C for one bag, ±0.3°C for two bags, and ±1.0°C for three bags. However, the consistency of temperature control declined from 99% for one bag to 95% for three bags. Completion signal reliability, vital for preventing uncontrolled thawing, ranged from 98% to 91%. We observed that user input accuracy demonstrated marginal variations, by decreasing from 94% for one bag to 88% for three bags. This suggests that, as the complexity of the operation increased, there was a minor reduction in precision in adhering to user-defined parameters. Visual inspection was mostly aligned with the completion signal.

Our study designed a cost-effective plasma thawer to overcome challenges in low-resource healthcare settings. Constructed with locally available components, the device demonstrates adaptability to resource constraints.

We assessed crucial aspects like thawing time, temperature control, completion signal reliability, user input accuracy, and visual inspection results. The cost comparison against industry benchmarks enhances the credibility of the findings. We included push buttons and an Arduino microcontroller for a

Table 3 Comparison of thawing characteristics of multiple bags

Characteristics	**1 Bag**	**2 Bags**	**3 Bags**
Average Thawing Time	12 minutes	14 minutes	16 minutes
Thawing Efficiency	86.6%	80%	73.3%
Temperature Control			
Deviation from Desired Range	±0.1°C	±0.3°C	±1.0°C
Consistency	99%	97%	95%
Completion Signal Reliability			
Prevented Uncontrolled Thawing	98%	95%	91%
User Input Accuracy			
Adherence to Specified Parameters	94%	90%	88%
Visual Inspection Results			
Correlation with Device Signals	96%	92%	90%

user-friendly interface, promoting practical implementation. Our plasma thawer compared to commercially available alternatives from different price ranges during the same period proved to be at least 10 times more cost-effective due to the utilization of locally available materials for its manufacturing and the avoidance of bearing import tariffs of around 21% [12]. (Table 4)

While this study successfully demonstrates the feasibility of a cost-effective plasma thawer, several limitations should be acknowledged. The device relies on a DS18B20 temperature sensor with a ±0.5°C accuracy which is adequate for general use but may not meet the precision required for critical thawing processes, particularly in clinical environments where tightly controlled temperature ranges are essential for preserving plasma proteins. Additionally, the study does not explore redundancy mechanisms for temperature regulation, such as backup sensors or relays, which could mitigate the risk of failure and ensure reliability during operation. The device's use of locally available materials, while cost-effective, may compromise its longevity and performance in high-demand clinical settings. We were not able to explore details regarding device lifespan or maintenance requirements.

Table 4 Cost comparison of our device with various plasma thawers available in the Market [13-15]

Plasma thawer type	**Current cost**
Boekel Scientific Plasma Thawer, 301000, 4 Bag (120V)	$7,895.72
DH4 QuickThaw® Plasma Thawing System	$1550
Barkey GmbH & Co. KG Plasma Thawer LPTU0008	$1,791
Cost-effective Plasma Thawer	PKR 8,000

The reliance on a water bath for thawing introduces the risk of bacterial contamination, which could be a concern in resource-limited environments with inconsistent sterilization protocols. We used a 1500-watt heater which may be a barrier in areas with inconsistent or expensive electricity availability. The manual input for temperature and time settings may be error-prone with minimal operator training.

Future research

Future work will address several of the limitations identified in this study. To improve temperature control precision, higher-accuracy sensors, such as PT100 or thermocouple sensors, will be evaluated to enhance performance in clinical applications [16]. Redundancy mechanisms, including dual sensors and backup relays, will be integrated to increase reliability and prevent potential failures during operation. The longevity and maintenance of the device will be explored through long-term testing to assess its durability in high-demand environments. To address the risk of microbial contamination, microbial assessments will be incorporated, and potential solutions such as closed-system designs or antimicrobial additives will be tested. , we plan to conduct advanced biochemical analyses in future studies to evaluate the impact of our thawing system on key coagulation factors, including Factor VIII, Prothrombin Time (PT), and Activated Partial Thromboplastin Time (aPTT). These tests will allow us to assess the preservation of coagulation factor activity and the overall therapeutic potency of the plasma post-thaw. We will also explore the effects of temperature fluctuations during the thawing process on these critical factors, ensuring that the device maintains plasma quality while preserving its intended clinical efficacy. The observed decline in temperature control consistency (from 99% for one bag to 95% for three) and thawing efficiency (from 86.6% to 73.3%) is an expected outcome given the prototype's current design and the constraints associated with its low-cost construction. These results still fall within acceptable limits for maintaining plasma quality, as the temperature remained within the optimal range (37-40°C) throughout the process, preventing protein denaturation or coagulation factor degradation. Importantly, the device was designed as a cost-effective solution tailored for low-resource settings, where scalability is often traded for affordability and accessibility. Future enhancements, such as improved water circulation and advanced control algorithms, can address these limitations, ensuring scalability without compromising cost-effectiveness. Energy efficiency will also be a priority, with alternative power solutions, such as solar panels or lower-wattage heating elements, being explored for off-grid and low-energy environments. Automation of temperature and time settings will be implemented to reduce operator errors and enhance usability, particularly in low-resource settings. Finally, comprehensive benchmarking against commercial thawing systems, including microwave thawers and closed-loop systems, will be conducted to compare thawing time, plasma quality, and overall performance, providing a clearer picture of the device's effectiveness and its potential as a viable alternative in resource-limited healthcare settings

4. Conclusion

We developed a cost-effective plasma thawer for low-resource settings. The device was able to thaw plasma within 12–16 minutes, with a temperature deviation of ±1°C. Completion signal reliability was 94.6%, preventing uncontrolled thawing, and plasma quality remained intact, free from protein denaturation. The device was 10 times more cost-effective than commercially available alternatives. The high cost of medical equipment in low- and middle-income countries limits access to essential healthcare technologies. This affordable solution offers a practical alternative to expensive commercial thawers, addressing both cost and operator training challenges. It has the potential to improve transfusion practices in resource-limited settings, ensuring safe and efficient plasma thawing.

Future work will focus on validating the device in diverse conditions, assessing its impact on plasma coagulation and hemostatic potency, and enhancing automation features for greater user-friendliness. Further cost-reduction strategies will also be explored to increase accessibility.

AUTHOR CONTRIBUTIONS

The study was conceptualized and designed by S.S, M.D.M and A.Z.R. M.A.H and M.D.M performed the construction of the device and the acquisition of data. A.Z.R and S.S. wrote the first draft of the manuscript that was reviewed by all authors. All authors read and approved the final manuscript. M.A.H and S.A.Q critically assessed the work for crucial intellectual substance and provided the final approval. The funding for this initiative was organized in part by S.A.Q.

DATA AVAILABILTY STATEMENT

The dataset accompanying this manuscript will be available from the corresponding author upon reasonable request.

CONFLICT OF INTEREST

The authors declare no conflicts of interest exist.

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