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Evaluating the Safety of Stress-Exposed Normal Saline in a Simulated Prehospital Emergency Environment

Mustafa Al-Khaldi[1], Samer Aziz[1], Raad Hussein[1]*

[1]Department of Medical Sciences, Faculty of Medicine, University of Mosul, Mosul, Iraq.

***E-mail** ✉ raad.hussein.med@yahoo.com

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ABSTRACT

There is a shortage of evidence regarding the stability and safe use of normal saline stored under stressful conditions within ambulances. Our objective was to evaluate how exposure to extreme temperature fluctuations affects the stability of normal saline and its compatibility with the packaging materials. Ninety-six polyolefin bags of normal saline were exposed to constant temperatures of 22, 50, or 70 °C, or to cycles of 70 °C for 8 hours and 22 °C for 16 hours. Bags were sampled at set intervals—up to 72 hours for the short-term study and weekly for four weeks in the long-term study. Solutions were inspected for crystallization, discoloration, turbidity, and pH changes, and samples were analyzed for sodium and chloride content. No precipitation, discoloration, or turbidity was observed in any of the normal saline bags. The mean pH values measured were 5.59 at 22 °C, 5.73 at 50 °C, 5.86 at 70 °C, and 5.79 under cyclic temperature conditions. Across both short- and long-term studies, sodium concentrations ranged from 100.2% to 111.27%, while chloride levels remained between 99.04% and 110.95%. No evidence of plastic component leaching from the polyolefin containers into the saline solution was detected. Sodium and chloride concentrations in normal saline remained stable and showed compatibility with polyolefin bags after exposure to simulated continuous and cyclic extreme temperatures for approximately one month. However, the influence of storage within ambulance cabinets across different seasons in arid regions still requires real-world investigation to validate these findings.

Keywords: 0.9% sodium chloride, Normal saline, Stability, Temperature, Prehospital, Emergency medical setting

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Introduction

In the United States, 0.9% sodium chloride solution—commonly referred to as normal saline—is one of the most frequently administered intravenous fluids, with annual usage exceeding 200 million liters [1, 2]. Since its early adoption, it has become a cornerstone of clinical care and remains the dominant crystalloid used in hospitals and emergency settings [3]. Clinically, it serves primarily to restore or maintain hydration [4, 5]. Cold normal saline has been employed to initiate therapeutic hypothermia [6, 7], whereas warmed saline is infused to help reverse accidental hypothermia [8, 9]. It is also routinely used as a diluent or carrier solution when intravenous medications require an appropriate vehicle for administration [10].

Normal saline provides equal concentrations of sodium and chloride. Each liter of the United States Pharmacopeia (USP) 0.9% formulation contains 154 mEq of each ion, has an osmolarity of 308 mOsmol/L, and exhibits a pH of approximately 5.6, within an allowable range of 4.5–7.0 [11]. Sodium is the predominant extracellular electrolyte and is central to fluid balance and electrolyte distribution. Chloride contributes to physiological buffering in lung and tissue environments and plays a role in enabling hemoglobin to associate with oxygen or carbon dioxide [12].

To safeguard pharmaceutical quality, the USP specifies acceptable conditions for storing and transporting each medication. However, adhering to these standards is often difficult in the prehospital emergency medical service

(EMS) environment, where medications may be exposed to uncontrollable elements such as light, humidity, vibration, and fluctuating temperatures—the latter being the most extensively investigated factor. Our earlier work demonstrated that epinephrine degrades significantly when subjected to extreme heat, posing risks of subtherapeutic dosing during critical emergencies [13]. Several additional studies have examined epinephrine's stability outside recommended conditions in various dosage forms [14–16]. Other drugs, including amiodarone, rocuronium, fentanyl, succinylcholine, and epinephrine, have been shown to maintain acceptable potency for up to a year in EMS vehicles exposed to real ambient temperatures ranging from 13.9 °C to 33.9 °C [17]. Ketamine, diazepam, and midazolam also retain relative stability despite long-term storage in high-heat settings, with mean kinetic temperatures recorded at 27.1 °C for ketamine and 31.6 °C for diazepam and midazolam [18, 19]. Studies involving air medical transport have similarly reported temperature-induced degradation, although drug concentrations generally remained above the acceptable 90% limit, despite exposure up to 38.1 °C [20]. A broader review of prehospital medications concluded that actual storage temperatures routinely fail to meet USP recommendations and emphasized the need for further investigation into how uncontrolled EMS environments affect medication stability [21].

In the Gulf Cooperation Council region—and specifically Qatar—summer conditions are particularly extreme, with temperatures surpassing 50 °C and relative humidity reaching about 95%, according to the national Civil Aviation Authority. Although the ambulance fleet is modern and air-conditioned, the interior environment rapidly heats up whenever doors are opened or the engine is shut off. Consequently, medications and fluids stored inside are routinely exposed to environmental stressors [22]. Despite this, data on the thermal stability of normal saline in prehospital settings within the Middle East and North Africa (MENA) region remain minimal [23].

Given these conditions, evaluating how storage duration and temperature affect normal saline in operational ambulances is necessary. It is equally important to determine whether heat exposure influences the interaction between saline and the plastic materials used in its packaging [24]. Such packaging may be made of polyvinyl chloride (PVC) or polyolefin (PO), the latter produced from alkene-based polymers and widely used in IV containers internationally [25]. The present study was designed to examine how both short- and long-term temperature exposure impacts the stability of normal saline and to assess the compatibility of polyolefin (PLÜMAT) bags with saline, defined as remaining free from leached plastic constituents. This represents the first investigation to explore these issues in a simulated prehospital thermal environment.

Materials and Methods

Apparatus and conditions

Quantification of sodium and chloride ions was performed using ion exchange chromatography (IEC) on a Metrohm 850 Professional IEC instrument (Herisau, Switzerland) following established analytical procedures [26–28]. **Table 1** outlines the optimized chromatographic conditions used for these measurements.

Table1. Optimized ion exchange chromatography parameters.

Parameter	Value
Eluent	3.2 mM Na_2CO_3/1.0 mM $NaHCO_3$ (anions) 0.7 mM dipicolinic acid (DPA)/2.8 mM HNO_3 (cations)
Flow	0.7 mL/min (anions) 0.9 mL/min (cations)
Columns	Metrosep A Supp 5–150/4.0 (anions) Metrosep C_4 – 150/4.0 (cations)
Temperature	30 °C
Sample loop	250 µL
Injection volume	20 µL (anions) and 10 µL (cations)
Recording Time	22.0 min (anions) and 13.0 min (cations)
Suppressor	0.1 M H_3PO_4
Detector	Conductivity detector

Reagents and materials

Sodium and chloride stock standards (1000 mg/L) and analytical-grade reagents—dipicolinic acid, sodium bicarbonate, sodium carbonate, nitric acid, and phosphoric acid—were purchased from Sigma-Aldrich

(Darmstadt, Germany). Eluents were vacuum-filtered through 0.45 µm nylon filters (Pall, Michigan, USA) using a Handling Systems setup (Kontes, Vineland, NJ) and degassed in an XUB ultrasonic bath (Royston, UK). All solutions were prepared with ultrapure Milli-Q water (Millipore, Billerica, MA, USA).

Sample collection and preparation

For this study, 0.9% sodium chloride in 500 mL polyolefin (PLÜMAT) infusion bags was procured from Qatar Pharma (Doha, Qatar), all belonging to the same production batch (BN:1929013008). The 96 bags were divided into four groups of 24 according to the temperature conditions to which they were exposed **(Figure 1).** Storage included short-term durations of 12, 24, 48, and 72 hours and long-term periods of 1, 2, 3, and 4 weeks. Bags were maintained either at constant temperatures of 22, 50, or 70 °C or under a cyclic regimen alternating between 70 °C for 8 hours and 22 °C for 16 hours. Using a 1 mL syringe, aliquots of saline were drawn from each bag's access port and stored at 4 °C until analysis. For measurement of sodium and chloride, 20 µL of each sample was diluted with 12 mL of distilled water and analyzed using a Metrohm 850 Professional ion exchange chromatography (IEC) system.

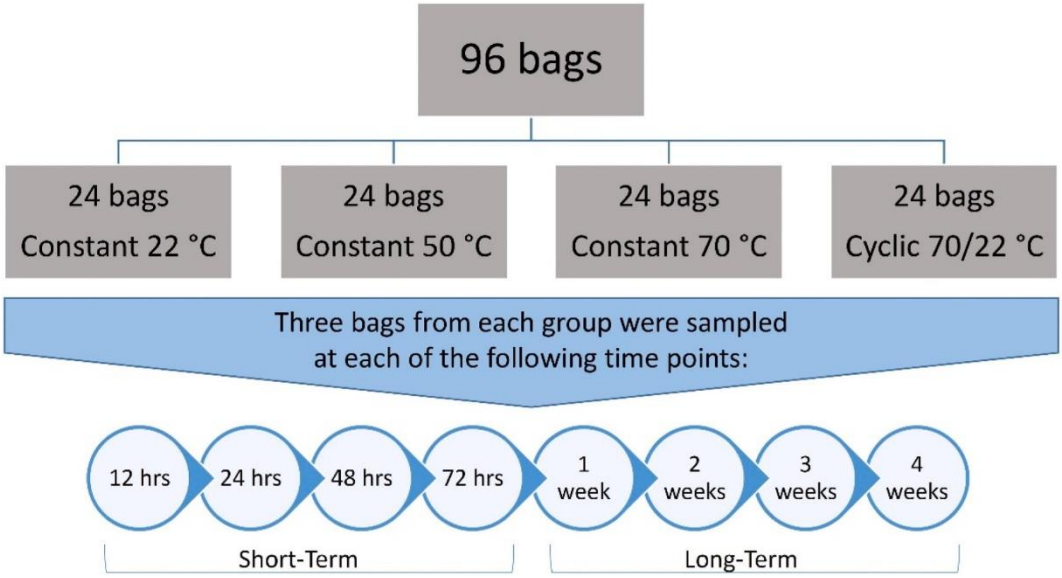


Figure 1. Schematic representation of normal saline groups and their respective sampling intervals.

Physical stability

The physical integrity of the normal saline samples was assessed through visual inspection. Before each sampling, the solutions were brought to room temperature and gently inverted to ensure homogeneity. Each sample was then examined against both black and white backgrounds to detect any particulate matter, turbidity, or changes in color. Additionally, pH measurements were conducted at room temperature using an Oakton pH 2700 Meter (Oakton Instruments, Illinois, USA). The instrument was calibrated with standard buffer solutions at pH 4.00, 7.00, and 10.00 prior to analysis.

Migration of plastic components

To assess whether compounds from the polyolefin (PO) bag—such as monomers, plasticizers, polymerization initiators, or stabilizing agents—were migrating into the normal saline, the solution was analyzed using ultraviolet–visible (UV–Vis) spectroscopy. Spectral scans were performed over a 200–500 nm wavelength range with a Varian Cary 50 Conc UV–Vis Spectrophotometer (Varian, Victoria, Australia).

Results and Discussion

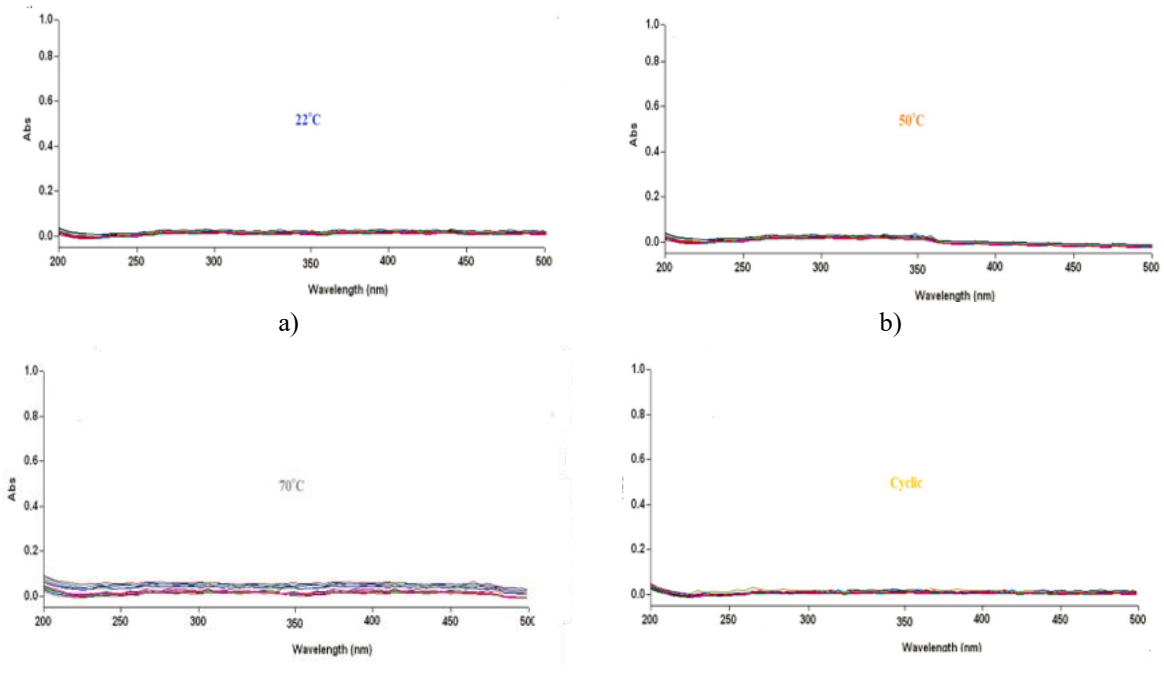
Across all groups of normal saline exposed to varying temperatures and durations, the solutions remained clear, free of visible precipitates, and showed no color changes, indicating that their physical stability was preserved. Slight swelling of the polyolefin (PLÜMAT) bags was noted at 50 °C, while more pronounced bulging occurred

at 70 °C and under cyclic temperature conditions **(Figure 2)**, likely due to water vapor formation during prolonged heating over the 28-day period.

a) b) c) d)

Figure 2. Swelling of polyolefin (PLÜMAT) normal saline bags under different temperature conditions: (a) 22 °C, (b) 50 °C, (c) 70 °C, and (d) cyclic temperature exposure.

The potential migration of plastic constituents—including olefinic monomers, plasticizers, polymerization initiators, and stabilizing additives—was evaluated using UV–Vis absorption spectroscopy, scanning the 200–500 nm range, following the method of Chang *et al*. (2010) with slight modifications **(Figure 3)** [25]. No absorbance was detected in normal saline stored at 50 °C, 70 °C, or under cyclic temperature conditions compared with the solution stored at 22 °C. This indicates that none of the plastic additives or other leachable components were transferred from the polyolefin bags into the saline.



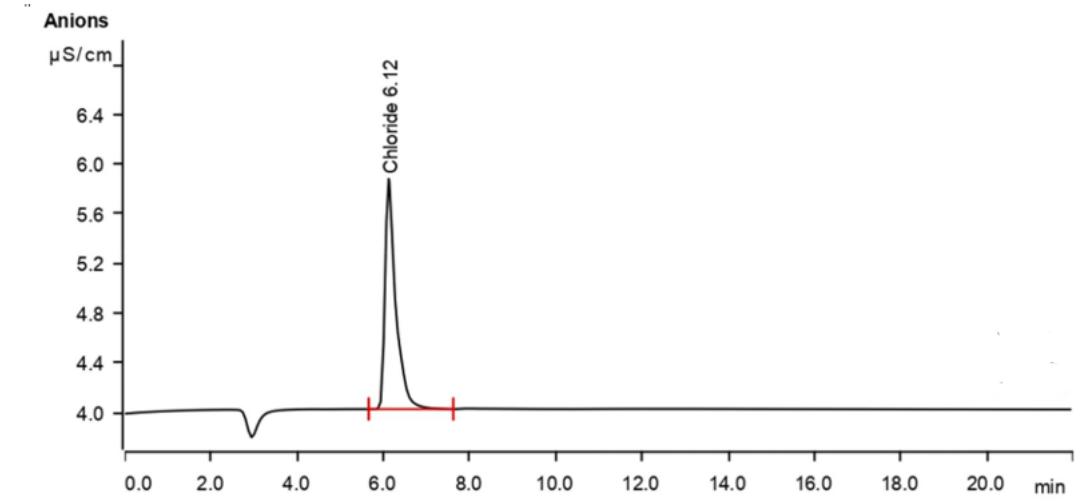
a) b)

d) e)

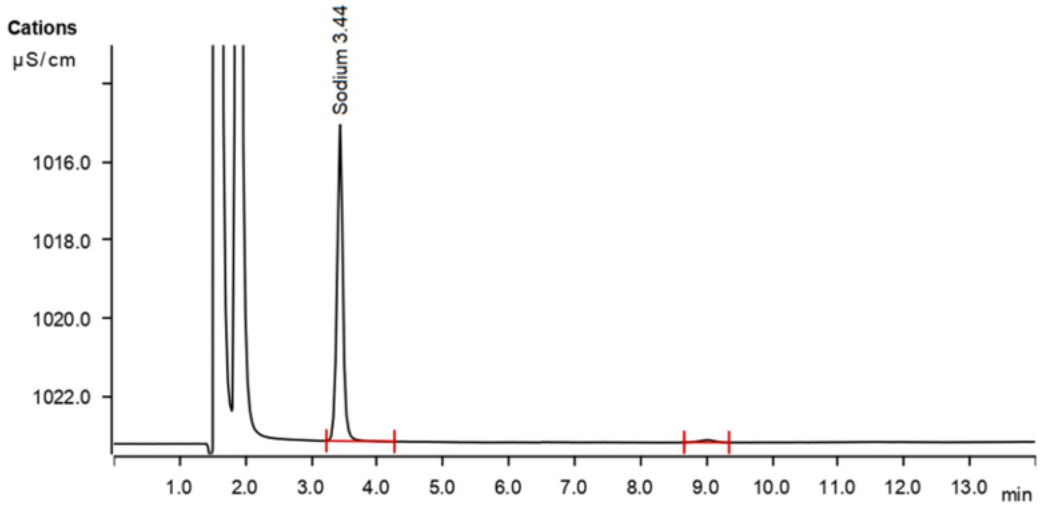
Figure 3. UV–Vis spectra of 500 mL normal saline stored in polyolefin (PLÜMAT) bags under different thermal conditions for 28 days: (a) 22 °C, (b) 50 °C, (c) 70 °C, and (d) cyclic temperature exposure.

To assess thermal stability, the concentrations of chloride **(Figure 4a)** and sodium **(Figure 4b)** were compared to their initial values, which were defined as 100%. Subsequent measurements were expressed as percentages of these baseline concentrations, with results reported as mean ± SD for three replicates. The initial pH of the saline

ranged between 4.5 and 7.0. Detailed results of both short-term and long-term thermal exposure are summarized in **Tables 2 and 3.**



a)



b)

Figure 4. Chromatographic profiles illustrating ion analysis of normal saline: (a) chloride detection at 10 mg/L using anion exchange with a sodium carbonate–sodium bicarbonate eluent, and (b) sodium detection at 10 mg/L via cation exchange using a dipicolinic acid–nitric acid eluent.

Table 2. Short-term retention of sodium and chloride in normal saline (n = 48), expressed as the proportion of the initial concentrations remaining after the exposure period.

T (°C)	Na^+ levels (%Remaining±SD) Time (Hours)				C l^- levels (%Remaining±SD) Time (Hours)			
	12	24	48	72	12	24	48	72
22	100.9 ± 0.8	100.2 ± 0.9	100.6 ± 0.5	100.8 ± 0.7	99.3 ± 0.7	99.0 ± 0.6	99.5 ± 0.7	99.4 ± 0.4
50	104.3 ± 1.5	104.7 ± 1.9	104.7 ± 0.8	105.3 ± 0.3	101.3 ± 1.8	100.4 ± 1.7	100.1 ± 0.7	101.8 ± 0.7
70	106.3 ± 0.8	110.2 ± 0.8	110.1 ± 1.5	110.7 ± 0.8	100.1 ± 1.4	101.7 ± 1.3	102.1 ± 1.7	102.0 ± 0.7
Cyclic	107.1 ± 1.6	105.7 ± 1.1	105.8 ± 1.6	107.9 ± 0.7	100.5 ± 1.6	99.8 ± 1.8	100.0 ± 1.6	100.9 ± 0.9

Table 3. Long-term retention of sodium and chloride in normal saline (n = 48), expressed as the percentage of the original concentrations remaining over the study period.

T (°C)	Na^+ levels (%Remaining±SD) Time (Weeks)				C l^- levels (%Remaining±SD) Time (Weeks)			
	1	2	3	4	1	2	3	4

22	103.4 ± 0.6	103.7 ± 2.3	103.0 ± 1.7	101.9 ± 0.9	101.9 ± 1.1	101.6 ± 1.7	99.0 ± 0.9	100.0 ± 0.8
50	102.4 ± 0.8	101.9 ± 0.8	109.8 ± 1.8	104.5 ± 4.2	100.8 ± 1.0	101.6 ± 1.3	109.9 ± 1.3	102.8 ± 2.0
70	105.8 ± 1.1	104.7 ± 2.5	109.9 ± 2.0	111.3 ± 2.6	103.7 ± 0.8	104.0 ± 2.4	108.8 ± 2.4	111.0 ± 1.6
Cyclic	103.7 ± 1.8	104.5 ± 1.6	105.4 ± 1.5	105.6 ± 1.7	103.7 ± 1.4	103.3 ± 1.1	105.5 ± 0.8	105.0 ± 1.6

A considerable body of research has questioned how well EMS medications tolerate the extreme environments in which they are often stored. One notable investigation by Helm M *et al*. tracked real-world temperature exposures in helicopters and ground emergency vehicles over alternating summer and winter intervals in southern Germany [29]. Temperatures fluctuated dramatically, from −13.2 °C in winter to peaks above 50 °C in summer, and exceeded the recommended storage ceiling of 25 °C for nearly half of the observation period. Their study highlighted the need for temperature-controlled storage systems but did not explore the chemical fate of the medications themselves. Additional work in a National Park Service setting later demonstrated that certain drugs deteriorate at temperature extremes, though not always in a uniform or heat-dependent pattern [30].

In climates that are both hot and arid, the question of compatibility between IV solutions and their packaging becomes just as important as thermal stability. Our study was designed to evaluate these two aspects over a 28-day period at several temperature conditions, although humidity could not be simulated alongside heat. Published evidence specifically examining how normal saline behaves inside polyolefin (PLÜMAT) bags under extreme thermal stress is scarce. Given the possibility that plastics may release additives or structural components into stored solutions, we assessed potential leaching by incubating the bags at 22, 50, and 70 °C as well as under a daily heating–cooling cycle. UV–Vis analysis revealed no absorbance at 226 nm, where phthalate-related compounds typically appear [31], nor at 320 nm, associated with other packaging-derived substances [25]. Chang *et al*. previously discussed comparable issues for anticancer drugs stored in PVC or polyolefin containers [25]. Our results indicate that the PLÜMAT material released no detectable plastic-associated contaminants into normal saline **(Figure 3),** aligning with findings from Trissel *et al*., who reported broad compatibility of polyolefin bags with multiple drug formulations [32].

Throughout the study, the saline remained clear, particle-free, and within an acceptable pH range. Temperature-related shifts in pH were minor, with means of 5.59 ± 0.08 at 22 °C, 5.73 ± 0.04 at 50 °C, 5.86 ± 0.02 at 70 °C, and 5.79 ± 0.03 under cyclic heating, all comfortably falling within the pharmacopeial range of 4.5–7.0. Measurements of sodium and chloride showed that their concentrations largely remained stable, deviating slightly—generally within an 11% margin—which we attribute to bag expansion at higher temperatures rather than loss of ions. In values obtained across both short- and long-term sampling periods, sodium remained between 100–111% of its initial concentration and chloride between roughly 99–111%. The close agreement between bags **(Tables 2 and 3)** suggests that no appreciable adsorption of electrolytes onto the polyolefin surface occurred. Taken together, these findings indicate that the chemical and physical integrity of normal saline is preserved in 500 mL polyolefin (PLÜMAT) containers for at least 28 days, even when subjected to temperatures up to 70 °C. Under the thermal conditions often encountered in ambulances, saline stored in these bags should therefore remain suitable for patient use. These results support retaining, rather than routinely discarding, saline bags that have been stored for extended periods in emergency vehicles, which could help reduce unnecessary waste and associated costs.

Limitations

Although our analysis focused on chemical stability, other aspects of product quality—particularly biological and microbiological stability—were not examined. The simulated temperature exposures used here do not fully capture the complexity of actual field conditions. For a more accurate assessment, saline bags should be evaluated inside operational ambulances during peak summer conditions in arid regions [33].

Conclusion

Across all tested temperature conditions, no evidence of plastic-derived substances or surfactants was detected in the saline. The fluid maintained its visual clarity, and electrolyte concentrations remained within clinically acceptable limits. Polyolefin (PLÜMAT) bags therefore appear to be a safe and compatible packaging option for normal saline exposed to high temperatures for periods up to 28 days. Solutions stored at room temperature were indistinguishable in quality from those exposed to 50 °C, 70 °C, or daily temperature cycling. While these findings

support the safe use of such bags in prehospital environments, further verification under authentic environmental conditions is warranted.

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Ethics Statement: None

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