BPB Reports

Report

Evaluation of the Decontamination Efficacy of Hypochlorous Acid Water on Surfaces With Antineoplastic Drugs: A Comparative Study of 5-Fluorouracil, Gemcitabine, and Paclitaxel

Yuma Nonomiya,[a,b,*] Yume Otsuka,[b] Makoto Hiraide,[c] Tomofumi Watanabe,[d] Hisanori Shimizu,[b] and Masakazu Yamaguchi[b]

[a]*Division of Pharmaceutical Care Sciences, Center for Social Pharmacy and Pharmaceutical Care Sciences, Keio University Faculty of Pharmacy, 1-5-30 Shibakoen, Minato-ku, Tokyo 105-8512, Japan;* [b]*Department of Pharmacy, Cancer Institute Hospital, Japanese Foundation for Cancer Research, 3-8-31 Ariake, Koto-ku, Tokyo 135-8550, Japan;* [c]*Department of Clinical Assessment, Tokyo University of Pharmacy and Life Sciences, 1432-1 Horinouchi, Hachioji, Tokyo 192-0392, Japan;* [d]*Division of Applied Pharmaceutical Education and Research, School of Pharmacy and Pharmaceutical Sciences, Hoshi University, 2-4-41 Ebara, Shinagawa-ku, Tokyo, 142-8501, Japan*

Received March 23, 2026; Accepted June 2, 2026

Environmental contamination from antineoplastic drugs poses a significant occupational health risk to healthcare professionals. Herein, we evaluated the efficacy of a recently developed decontamination method using hypochlorous acid (HClO) water and alkaline electrolyzed water (AEW) compared to conventional cleaning, focusing on the physicochemical properties of target drugs. Decontamination efficacy was assessed on work desks and clean benches using an ATP bioluminescence assay (RLU values). Additionally, a wipe test was conducted on stainless-steel plates contaminated with 5-fluorouracil (5-FU), gemcitabine (GEM), and paclitaxel (PTX) to quantify residual drug concentrations after cleaning with either distilled water/ethanol or HClO/AEW. Cleaning with HClO and AEW significantly reduced the RLU values compared to those from conventional cleaning (distilled water and ethanol) ($p < 0.05$), achieving levels below the standard threshold of 200 RLU. Regarding the wipe test, HClO and AEW demonstrated superior removal efficacy for the hydrophilic drugs 5-FU and GEM ($p < 0.05$). Conversely, residual levels of the highly lipophilic drug PTX (log P = 2.5) were significantly higher following HClO/AEW cleaning than those from the ethanol-based method. The combination of HClO and AEW provides excellent baseline cleanliness and is highly effective for decontaminating surfaces with hydrophilic antineoplastic drugs. However, its efficacy in removing lipophilic agents, such as PTX which may form hydrophobic films, is limited. These findings suggest that a multilayered decontamination strategy, such as HClO treatment with an ethanol wipe, is essential for comprehensive safety, and provide a scientific basis for selecting cleaning protocols based on the log P-values of handled hazardous drugs.

Key words antineoplastic drugs, hypochlorous acid, alkaline electrolyzed water, Wipe Test

INTRODUCTION

Most antineoplastic drugs exert cytotoxic effects on normal cells and antitumor effects on cancer cells.[1)] Furthermore, the risk of health hazards—including carcinogenicity, teratogenicity, and reproductive toxicity—resulting from exposure to these agents is well documented, highlighting the critical importance of occupational exposure measures for healthcare workers.[2)] To this end, it is essential for each medical facility to establish protocols tailored to their specific environment, guided by resources such as the "Guidelines for the Handling of Antineoplastic Drugs in Hospitals" issued by the Japanese Society of Hospital Pharmacists. Comprehensive strategies to mitigate exposure include the use of biological safety cabinets (BSCs), wearing personal protective equipment, and thorough surface decontamination.[3-4)] Specialized products formulated with sodium thiosulfate, sodium hydroxide, and sodium hypochlorite are commercially available and utilized in clinical settings for the decontamination of neoplastic agents.[5-6)] However, these agents are often unsuitable for routine daily cleaning owing to their corrosive nature and significant operational workload. Owing to this, a combination of distilled water and ethanol is commonly used for daily maintenance. Nevertheless, if drug residues are not fully removed by distilled water, the high volatility of ethanol may increase the risk of inhalation exposure to the remaining antineoplastic agents.

At the Pharmacy Department of Cancer Institute Hospital, Japanese Foundation for Cancer Research (JFCR), we

*To whom correspondence should be addressed. e-mail: nonomiya-ym@keio.jp

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installed a Hoshizaki Hand Disinfector (WOX-30WA-M2®; Hoshizaki Sales Co., Ltd., Nagoya, Japan), a certified highly acidic electrolyzed water generator (Certification Number: 302GBZX00059000), for hand disinfection before and after the preparation of antineoplastic drugs. We focused on the decontamination potential of hypochlorous acid (HClO) water (hereinafter referred to as HClO) and alkaline electrolyzed water (AEW) produced by this system. Previously, we demonstrated that cleaning with HClO and AEW significantly reduced the residual concentration of cyclophosphamide, an alkylating agent, compared to conventional cleaning with distilled water and ethanol.[7)]

On the background of our previous findings, this study evaluated the utility of a HClO and AEW cleaning protocol, focusing on three antineoplastic drugs with high clinical usage and distinct physicochemical properties: 5-fluorouracil (5-FU), gemcitabine (GEM), and paclitaxel (PTX).

MATERIAL AND METHODS

Hoshizaki Hand Disinfector (WOX-30WA-M2®WOX) Strongly acidic electrolyzed water (containing 0.015% HClO) was produced by the electrolysis of an aqueous sodium chloride solution. We used a modified WOX system that was specifically adapted to allow collection of discharged AEW (containing sodium hydroxide). Both HClO and AEW used in the experiments were collected immediately prior to use.

Decontamination Procedures Distilled water (Otsuka Pharmaceutical Co., Ltd., Tokyo, Japan) and Saraya Ethanol Cloth 80 (Medical Saraya, Osaka, Japan) were used. For cleaning with distilled water, 20 mL was impregnated into three sheets of sterile gauze (Sterile Osaki Medical Gauze, Tokyo, Japan) immediately before use. Ethanol cleaning then followed using sheets of Saraya Ethanol Cloth 80.

Regarding HClO/AEW cleaning, 30 mL of the solution discharged from the WOX system and impregnated into three sheets of gauze was used.

ATP Bioluminescence Assay A 10 × 10 cm (100 cm^2) area on desks and clean benches located in the compounding room of our hospital was designated as the measurement site. Both the work desk and clean bench surfaces were made of stainless steel (SUS304). Measurements were performed approximately 14 h after the last cleaning. The work desk was used for compounding preparations and routine laboratory work, while the clean bench was used for the preparation of sterile formulations. The surface was thoroughly wiped using LuciPac A3 Surface pre-moistened swabs (Kikkoman Biochemifa Co., Tokyo, Japan). The collected samples were analyzed using a dedicated luminometer (Lumitester Smart; Kikkoman Biochemifa Co., Tokyo, Japan) to determine ATP levels expressed in Relative Light Units (RLU). The experimental design was sequential in nature. Decontamination efficacy was first evaluated on the work desk to assess the effect of HClO water alone. Based on these results, the investigation was extended to the clean bench, where AEW was additionally incorporated as a neutralization step to prevent corrosion of stainless steel surfaces caused by the acidic HClO water.

Preparation of a Contamination Model Stainless-steel plates (SUS304, 30 × 30 cm) of the same material as that used in BSCs and on clean benches were used in this study. Solutions of 5-FU, GEM, and PTX (FUJIFILM Wako Pure Chemical Corporation, Osaka, Japan) were prepared at concentrations of 1, 10, and 100 µg/mL. To create the contamination model, 100 µL of each solution was spiked onto 10 separate spots on a stainless steel plate, resulting in a total applied amount of 1, 10, and 100 µg per plate for the 1, 10, and 100 µg/mL solutions, respectively. Since new stainless steel plates were used, the spiked amounts represent the initial contamination levels, eliminating the need for separate baseline measurements. The plates were allowed to dry for 24 h prior to use as antineoplastic drug-contaminated surface models.

Wipe Test for Surface Contamination The contaminated stainless-steel plates prepared above were cleaned using two different methods: the conventional method (distilled water and ethanol) and the HClO and AEW approach. As depicted in Fig. 1, the surface of each plate was wiped using a single back-and-forth motion. Surface sampling was performed 24 h after cleaning using specialized gauze, following the wipe

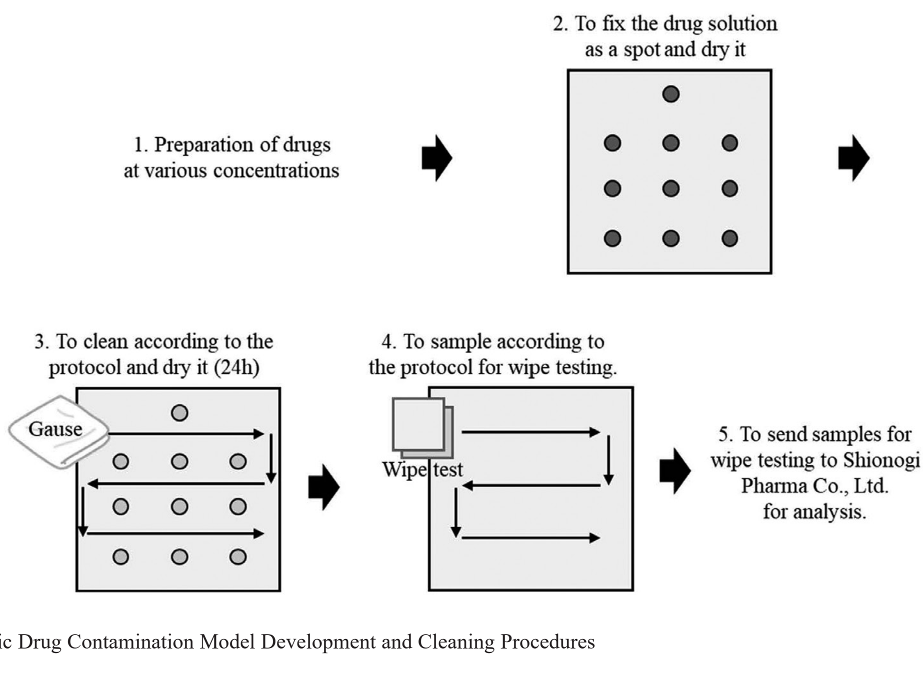

Fig. 1. Antineoplastic Drug Contamination Model Development and Cleaning Procedures

test protocol provided by Shionogi Pharma Co., Ltd. (Osaka, Japan). The collected gauze samples were subsequently sent to Shionogi Pharma Co., Ltd. for quantitative analysis of residual antineoplastic drugs.

Statistical Analysis RLU values obtained from the ATP bioluminescence assay were compared using Dunnett's test (n = 6 per group). For the wipe test, the Mann–Whitney test was used to compare residual drug concentrations (n = 3 per group), as the sample size was limited due to the constraints of outsourcing measurements to an external manufacturer (Shionogi Pharma Co., Ltd.), making the assumption of normality inappropriate. All statistical analyses were performed using SPSS version 24 software (IBM Corp., Armonk, NY, USA). Statistical significance was set at $p < 0.05$. Figures and tables were generated using Microsoft Excel (Microsoft Corp., Redmond, WA, USA) and R Studio version 2026.01.2 (Posit PBC, Boston, MA, USA) with R version 4.5.0 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Efficacy of Decontamination Using HClO Wiping the work desk with two sheets of ethanol showed a trend toward reduction in RLU values compared to cleaning with distilled water and ethanol. Notably, cleaning with HClO resulted in a significantly greater reduction in RLU values than those from conventional distilled water and ethanol cleaning ($p < 0.01$, Fig. 2A). Furthermore, cleaning of compounding benches with distilled water and ethanol yielded RLU levels below the standard threshold for smooth surfaces (200 RLU). The use of two ethanol sheets showed a trend toward further reduction in these values. More importantly, cleaning with HClO, as well as the combined use of HClO and AEW, demonstrated a significantly greater reduction in RLU values than from cleaning with distilled water and ethanol ($p = 0.02$ and $p = 0.01$, respectively). These findings suggest that decontamination using HClO is more effective than using conventional ethanol-based cleaning methods.

Verification of Residual Antineoplastic Drugs To verify the decontamination efficacy of the investigated methods, residual amounts of 5-FU, GEM, and PTX on stainless-steel plates were quantified after cleaning. For 5-FU, HClO and AEW significantly reduced the residual drug concentration across all concentrations (1, 10, 100 µg/mL) compared to cleaning with distilled water and ethanol (Fig. 3A). Regarding GEM, the residual concentration was significantly lower following cleaning with HClO and AEW at a concentration of 100 µg/mL. Although the differences were not statistically significant in the 1 and 10 µg/mL groups, a clear downward trend in residual levels was observed with the use of HClO and AEW (Fig. 3B).

Contrarily, the residual amount of PTX was significantly higher after cleaning with HClO and AEW than with distilled water and ethanol (Fig. 3C).

DISCUSSION

In this study, we evaluated environmental decontamination methods in both non-sterile and sterile settings using HClO, which was originally developed for hand disinfection. On work desks in the non-sterile environment, cleaning with HClO resulted in a more pronounced reduction in RLU values than conventional cleaning using distilled water and ethanol. Furthermore, on a clean bench within the sterile environment, the application of HClO alone, as well as the combined use of HClO and AEW, achieved a significantly greater reduction in RLU levels than traditional wiping methods. These results demonstrate that electrolyzed water possesses superior baseline cleaning efficacy for organic matter to standard protocols.

The RLU values measured using the ATP bioluminescence assay represent the total luminescence generated from the reaction between the reagent and ATP, ADP, and AMP. Consequently, a higher RLU value indicates a greater accumulation of organic residue. According to the standards established by Kikkoman Corp., the benchmark for cleanliness on smooth surfaces, such as stainless steel and glass, is <= 200 RLU. For uneven or easily scratched resin surfaces, the threshold is <= 500 RLU, and for hand surfaces, it is <= 2,000 RLU. Herein, the RLU values obtained after cleaning with distilled water and ethanol were below the established thresholds, confirming

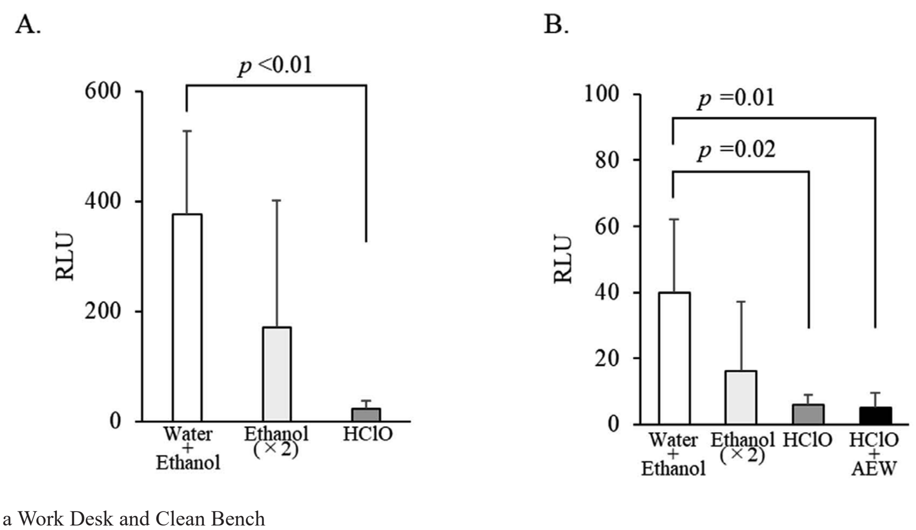

Fig. 2. RLU Values of a Work Desk and Clean Bench

RLU values were measured after performing different cleaning procedures (distilled water + ethanol, ethanol alone, HClO alone, and HClO + AEW) on (A) a work desk and (B) clean bench. Statistical analyses were performed using Dunnett's test. n=6 per group. Data are presented as the mean of six measurements taken at different locations, with error bars representing the standard error of the mean (SEM).

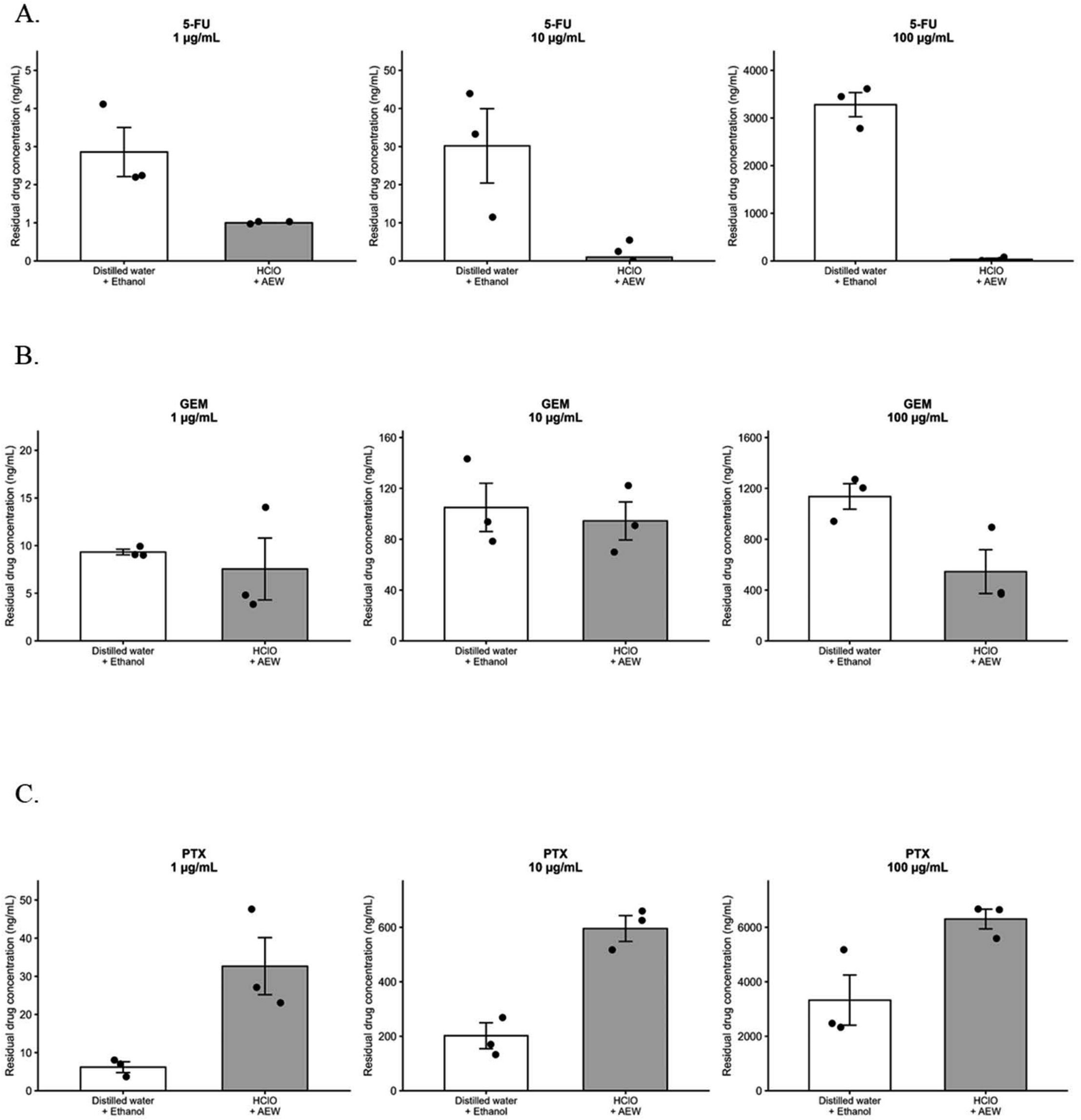

Fig. 3. Efficacy of Cleaning 5-FU, GEM, and PTX with HClO and AEW.

Residual drug concentrations were quantified using a wipe test after cleaning with either distilled water + ethanol or HClO + AEW. n=3 per group. Data are presented as the mean ± SD, with individual data points shown. Statistical significance was determined using the Mann–Whitney U test.

that conventional cleaning methods can maintain a sufficiently sanitary environment in clinical practice. As depicted in Fig. 2A and 2B, the use of HClO resulted in a further reduction in RLU values, suggesting that this method can maintain a higher level of environmental cleanliness. Previous studies reported that the disinfectant efficacy of surface wiping with HClO is comparable to that of ethanol.[8] Furthermore, investigations using feline calicivirus as a surrogate for norovirus demonstrated that electrolyzed water possesses potent inactivation capabilities and high removal and inactivation efficacy on medical devices, kitchen utensils, and hand surfaces.[9] These findings suggest that our cleaning protocol utilizing HClO is capable of removing organic substances previously unattainable with conventional distilled water and ethanol, thereby achieving a more pronounced reduction in RLU values.

However, our findings suggest that residual antineoplastic drug levels do not necessarily correlate with RLU values. This discrepancy is a consequence of the ATP bioluminescence assay detecting total organic matter, whereas the wipe test quantifies the target drug molecule. Previous studies reported that HClO effectively removes organic contaminants from environmental surfaces. Therefore, we propose that the use of HClO creates an optimal environment for the removal and degradation of antineoplastic drugs. By effectively stripping away the organic film composed of proteins and other debris that often shield drug residues, HClO may facilitate a more direct interaction between the cleaning agent and drug molecules, thereby enhancing overall decontamination efficacy.

Furthermore, results from the wipe test revealed that while cleaning with HClO and AEW provided significant removal of 5-FU and GEM, residual levels of PTX were noted. This discrepancy may be attributed to the differing physicochemical properties of each drug, particularly their lipophilicity, as indicated by their n-octanol/water partition coefficients (log P values).[10-11] The log P values of 5-FU and GEM are -0.9 and -1.5, respectively, indicating high hydrophilicity.[12-13] These drugs therefore react rapidly with aqueous HClO solutions, resulting in efficient oxidative degradation. In contrast, PTX has a log P value of 2.5,[14] implying hydrophobicity. Given these chemical characteristics, it is inevitable that ethanol-based wiping is superior for the removal of such lipophilic substances. PTX likely forms a hydrophobic thin film on environmental surfaces, which may have inhibited its molecular contact with the aqueous cleaning agent (HClO), resulting in higher residual levels.

Previous research demonstrated the efficacy of HClO against cyclophosphamide (log P = 0.6).[7,15] However, our results suggest that a single cleaning agent may be insufficient for highly lipophilic agents such as PTX. As expected, ethanol demonstrated superior removal of lipophilic drugs, such as PTX, because of its inherently low affinity for water. Therefore, implementing a final ethanol wipe after the electrolyzed water treatment is highly justified and offers significant practical advantages. This multistep approach ensures a more definitive elimination of residual lipophilic contaminants, such as PTX, while simultaneously achieving environmental disinfection and moisture removal to prevent corrosion of stainless-steel surfaces. It is speculated that in this synergistic approach, HClO and AEW would oxidatively degrade hydrophilic drugs and remove organic debris, whereas the subsequent ethanol wipe effectively dissolves and eliminates residual lipophilic contaminants.

This study has three primary limitations. Firstly, the number of antineoplastic drugs evaluated was limited. Although the investigated agents are frequently used in clinical practice, many other hazardous drugs with diverse chemical properties, such as anthracyclines (e.g., doxorubicin) and platinum-based compounds (e.g., cisplatin), are routinely handled. Further investigations are required to verify the efficacy of HClO across a wider range of pharmacological agents. Second, the experiments were conducted using stainless-steel plates of the same material as that used for BSCs. To ensure the comprehensive protection of healthcare workers from occupational exposure, decontamination efficacy on various materials and surfaces commonly found in clinical settings should be examined. Lastly, we were unable to determine whether the reduction in residual 5-FU and GEM concentrations resulted from physical removal through wiping or chemical degradation by HClO. Clarification of the specific mechanisms remains a topic for future research. Additionally, the wipe test employed in this study was designed to compare relative decontamination efficiency under identical conditions, rather than to determine the absolute recovery rate of each drug. As demonstrated by the differing decontamination efficacy observed across drugs with distinct physicochemical properties (log P values), the recovery efficiency of gauze wiping may also vary depending on these properties. However, since the gauze-based sampling procedure was identical in both cleaning groups, any such variation would affect both groups equally, preserving the validity of relative comparisons. Future studies should include validation of recovery efficiency for each drug to enable more accurate quantitative assessment.

In summary, compared to conventional cleaning using distilled water and ethanol, the combined application of HClO and AEW achieves superior environmental cleanliness and exerts highly effective decontamination, particularly for hydrophilic antineoplastic agents. Although challenges remain regarding the removal of lipophilic drugs, these findings provide essential baseline data for establishing multifaceted decontamination protocols tailored to the physicochemical properties of handled agents. Ultimately, this approach is expected to contribute significantly to the reduction of occupational exposure among healthcare professionals. Furthermore, it is crucial to investigate whether the chemical reactions between electrolyzed water and antineoplastic drugs produce secondary byproducts that may pose risks to human health. Beyond merely reducing residual drug levels, future studies must incorporate structural analyses to identify reaction intermediates and evaluate their safety profiles to ensure safe implementation of this decontamination method in clinical practice.

Funding This work was supported by the KP-kai Naomi Hoshino Memorial Grant for Pharmaceutical Research and Activities.

Conflict of interest The authors declare no conflict of interest.

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