Clin. Lab. 2026;72:XXX-XXX

ORIGINAL ARTICLE

Development and Evaluation of an LC-MS/MS Method for Determining Paraquat and Diquat in Human Plasma: a Retrospective Study

Jiayuan Wang [1, 2, 3], Bin Li [1, 2, 3], Ying Zhao [1, 2, 3], Limin Feng [1, 2, 3], Junshun Gao [4]

[1] *Department of Laboratory Medicine, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, P. R. China*
[2] *Zhejiang Key Laboratory of Clinical In Vitro Diagnostic Techniques, Hangzhou, Zhejiang, P. R. China*
[3] *Institute of Laboratory Medicine, Zhejiang University, Hangzhou, Zhejiang, P. R. China*
[4] *Cosmos Wisdom Biotech Co., Ltd., Hangzhou, Zhejiang, P. R. China*

SUMMARY

Background: **This study aimed to establish a high-performance liquid chromatography tandem mass spectrometry method for determining paraquat and diquat in human plasma and predict clinical outcomes.**
Methods: **Each plasma sample was subjected to methanol protein precipitation and passed through a hydrophilic column and was then analyzed by mass spectrometry to determine paraquat and diquat. Receiver operating characteristic curves were used to calculate herbicide poisoning severity indices and allow herbicide concentrations in plasma to be used to predict clinical outcomes.**
Results: **The responses to paraquat and diquat in plasma were strongly linear over the range of 20 - 10,000 ng/mL. The limit of quantitation and quality control samples met the required criteria. The paraquat and diquat poisoning severity index was significantly higher for the death group than the survival group ($p < 0.05$). The areas under the paraquat and diquat poisoning severity index receiver operating characteristic curves were 0.946 and 0.998, respectively, and the optimal clinical critical values were 22.84 and 15.64 (h·mg)/L, respectively, indicating good diagnostic performances for both herbicides.**
Conclusions: **The method is sensitive, accurate, quick, and specific, so it is highly recommended for clinical use.**
(Clin. Lab. 2026;72:xx-xx. DOI: 10.7754/Clin.Lab.2025.250311)

Correspondence:
Jiayuan Wang
Department of Laboratory Medicine
The First Affiliated Hospital
College of Medicine
Zhejiang Key Laboratory of Clinical
In Vitro Diagnostic Techniques
Zhejiang University
79, Qingchun Road
Hangzhou, 310003
Zhejiang
P. R. China
Phone: + 86 15267438103
Email: 1515113@zju.edu.cn

Manuscript accepted June 15, 2025

KEYWORDS

plasma concentration, paraquat, diquat, severity index of poisoning

INTRODUCTION

The extremely high mortality rate for people attempting suicide by ingesting paraquat has led to paraquat use and sale being prohibited in China. However, some rural households may still have paraquat, so it is still necessary to be vigilant for paraquat poisoning incidents. Diquat has become widely used as a substitute herbicide for paraquat in agricultural areas. However, the ingredient lists on herbicide containers are often unreliable, so it is necessary to be particularly cautious about the pos-

sibility of herbicides containing both diquat and paraquat.

Paraquat and diquat are bipyridine compounds with similar compositions that are very toxic to humans and animals [1]. Accidental or self-inflicted paraquat or diquat poisoning can damage the heart, lungs, liver, kidneys, and other important organs, and there are no specific antidotes [2]. Paraquat can be absorbed through various exposure routes, including the digestive tract, skin, and respiratory tract. Severe paraquat poisoning can progress to multiple organ dysfunction syndrome [3]. The lungs are the main target organs of paraquat, and severe respiratory system damage is the leading cause of death from paraquat poisoning [4]. Early manifestations of diquat and paraquat poisoning are similar, but diquat is less toxic compared to paraquat. The half-life of diquat is a sixth of the half-life of paraquat in the lungs [5]. Diquat causes slight, reversible harm to type I alveolar epithelial cells and no harm to type II alveolar epithelial cells [6]. Severe damage to the central nervous system caused by paraquat or diquat can lead to fatal complications such as central nervous system damage and refractory circulatory collapse [7].

Herbicide concentrations in plasma and poisoning severity indices at admission are often used when giving prognoses and predicting survival rates of poisoned patients. Rapid and accurate methods for simultaneously determining paraquat and diquat in tissue samples should be developed to acquire data so that clinicians can determine appropriate treatments. Many methods are available for determining paraquat and diquat, including capillary electrophoresis [8], spectrophotometry [9], liquid chromatography [10], gas chromatography [11], liquid chromatography tandem mass spectrometry [12], and others [13]. Here, we describe a method using triple quadrupole tandem mass spectrometry for simply and rapidly simultaneously determining paraquat and diquat in plasma. The method will allow physicians to objectively evaluate the severity of acute poisoning, establish a prognosis, and make clinical treatment intervention.

MATERIALS AND METHODS

Subjects

Plasma samples were obtained from individuals with paraquat or diquat poisoning, and blended plasma samples (to act as blank plasma controls) were collected from eight healthy individuals between March 2017 and February 2024. The age, admission time, and paraquat and diquat concentrations in plasma were monitored for each patient, and the poisoning severity index was calculated by multiplying the paraquat or diquat concentration in plasma (mg/L) by the time after exposure to paraquat or diquat (hours) [14-17]. A prognostic indicator based on mortality for 30 days after poisoning was used. Each patient included in the study had suffered oral paraquat or diquat poisoning and did not have a history of severe cardiovascular system, respiratory system, hepatic function, or renal function diseases. Patients with concurrent poisoning by other chemicals or trauma or who had abandoned treatment were excluded from the study.

Main instruments and reagents

The main instruments used were an Agilent 6495 triple quadrupole mass spectrometer (Agilent Technologies, Santa Clara, CA, USA), a 1290 Infinity II high-performance liquid chromatograph (Agilent Technologies), a 5424R frozen high-speed centrifuge (Eppendorf, Hamburg, Germany), and a Millipore Milli-Q ultrapure water generator (Merck, Darmstadt, Germany).

The reagents used were a 1 mg/mL stock paraquat standard (Toronto Research Chemicals, Toronto, Canada), a 1 mg/mL paraquat-d8 internal standard (Toronto Research Chemicals), a Dr. Ehrensorfer 100 µg/mL diquat stock standard (LGC, Teddington, UK), a Dr. Ehrensorfer 1 mg/mL diquat-d4 internal standard (LGC), HPLC-grade methanol (Thermo Fisher Scientific, Waltham, MA, USA), formic acid (Thermo Fisher Scientific), ammonium formate (Thermo Fisher Scientific), HPLC-grade acetonitrile (Merck), deionized water prepared in the laboratory, and herbicide-free plasma from healthy individuals (with no hemolysis, jaundice, or turbidity).

Reagent preparation

Standard solutions

A 100 µL aliquot of a 100 µg/mL paraquat solution and a 100 µL aliquot of a 100 µg/mL diquat solution were combined and diluted with methanol to 1 mL to give a blended stock solution comprising 10 µg/mL each of paraquat and diquat. Aliquots of this solution were diluted with methanol to give working standards at concentrations of 20, 50, 200, 500, 1,000, 2,000, 5,000, and 10,000 ng/mL.

Paraquat and diquat quality control solutions

Standards at concentrations of 1, 5, and 50 µg/mL were prepared by mixing appropriate amounts of the blended stock solution and methanol. A 5 µL aliquot of each solution was blended with 95 µL aliquots of blank plasma to give quality control solutions at low, medium, and high concentrations of 100, 500, and 5,000 ng/mL, respectively.

Internal standard working solutions

A 100 µL aliquot of a 1 mg/mL paraquat-d8 standard and a 100 µL aliquot of a 1 mg/mL diquat-d4 standard were blended and diluted with methanol to 1 mL to give a blended internal standard solution containing 10 µg/mL each of paraquat-d8 and diquat-d4. This internal standard solution was then diluted with methanol to prepare a 1,000 ng/mL working solution.

The blended stock standard and blended internal standard stock solutions were transferred to 1 mL ampoules and stored at -80°C. The working standards at various concentrations, the low, medium, and high concentration quality control samples, as well as the internal standard working solution, were stored at -20°C.

The HPLC-MS/MS system gave accurate results for diquat at concentrations between 20 and 10,000 ng/mL. When performing statistical analyses, diquat concentrations < 50 ng/mL but > 0 ng/mL were given the concentration 50 ng/mL, and concentrations >10,000 ng/mL were given the concentration 10,000 ng/mL.

Patient sample and quality control sample preparation

A 50 µL aliquot of the 1,000 ng/mL internal standard solution and 450 µL of methanol were added to 100 µL of a plasma sample or quality control sample. The mixture was vortexed for 2 minutes and then centrifuged at 15,871 × g for 10 minutes. A 400 µL aliquot of the supernatant and 200 µL of ultrapure water were then transferred to a vial, and 5 µL of the mixture was injected into the HPLC-MS/MS system.

Chromatographic conditions

The separation was achieved using a Waters XBridge BEH HILIC column (100 mm long, 2.1 mm i.d., 2.5 µm particle diameter), which was kept at 40°C. The mobile phase was a mixture of water containing 20 mmol/L ammonium formate and 0.1% formic acid (A) and acetonitrile (B), and the flow rate was 0.40 mL/min. The initial mobile phase mixture was 20% A and 80% B by volume, and was maintained for 1 minute, then the mixture was changed to 30% A and 70% B over 4 minutes. The composition was held for 1 minute, then gradually changed to 20% A and 80% B over the next minute, and finally maintained at this new ratio for another minute.

Mass spectrometer conditions

The mass spectrometer was operated in positive-ion multiple reaction monitoring mode. The optimized conditions were: nebulizer pressure 35 psi; drying gas flow rate 14 L/minute; drying gas temperature 360°C; HV capillary voltage 4,000 V. The injection volume was 5 µL. Each analyte was identified and quantified using quantification and qualification ions. The quantification ion for paraquat was *m/z* 186.1→171.1, the qualification ion for paraquat was *m/z* 186.1→77.1, and the quantification ion for paraquat-d8 was *m/z* 194.0→179.0. The quantification ion for diquat was *m/z* 183.1→157.1, the qualification ion for diquat was *m/z* 183.1→130.1, and the quantification ion for diquat-d4 was *m/z* 186.0→158.1. Identification of an analyte required the ratio between the quantification and qualification transition ions to be within ± 20% of the ratios for the calibration standards.

Statistical analysis

Statistical analyses were performed using Excel software (Microsoft, Redmond, WA, USA) and SPSS 21.0 software (IBM, Armonk, NY, USA). The mean, standard deviation, relative standard deviation, bias, and accuracy were calculated. Data following normal distribution were reported as the mean ± standard deviation, and *t*-tests were performed to compare data for pairs of sample groups. Data not following normal distribution were summarized as the median and quartiles, and non-parametric rank-sum tests were performed to compare data for different groups. Paraquat and diquat concentrations in plasma were plotted with sensitivity on the *y*-axis and specificity on the *x*-axis. The area under a receiver operating characteristic (ROC) curve for patient prognosis was determined using the SIPP, and a cutoff value was used to compare the predictive values of the two methods. A statistically significant difference was indicated by $p < 0.05$.

RESULTS

Methodology

Specificity

The product ion chromatograms of paraquat, paraquat-d8, diquat, and diquat-d4 acquired using the abovementioned instrument conditions are shown in Figure 1. In the chromatograms of herbicide-free plasma samples, no interfering peaks of endogenous substances were found near the retention times of paraquat and diquat. But in the chromatograms of the patients' plasma samples, peaks at the retention times of paraquat and diquat were detected, as shown in Figure 1.

Standard curves and quantitation limits

A 100 µL aliquot of each of the 20, 50, 200, 500, 1,000, 2,000, and 5,000 ng/mL paraquat and diquat working standards was added to each of a series of 100 µL aliquots of herbicide-free plasma, and the spiked samples were analyzed using the conditions described above. The responses to paraquat and diquat were linear in the concentration range 20 - 10,000 ng/mL, and the correlation coefficients (R) were 0.991 - 0.999. The typical regression equation was y = 2.567224, x - 0.015138 (R^2 = 0.997, n = 8). The limit of quantitation was 20 ng/mL.

Trueness

Quality control spiked-matrix samples at low, medium, and high concentrations were analyzed over 4 days; five samples at each concentration were analyzed, as shown in Table 1. The accuracy and precision of the method for determining paraquat and diquat in human plasma met the required criteria, as shown in Table 2.

Matrix effects

Matrix effects were assessed by analyzing 95 µL aliquots of herbicide-free plasma processed as described in section *'Patient sample and quality control sample preparation'* without adding internal standards. A 5 µL aliquot of the blended standard solution was added to each sample aliquot to give final paraquat and diquat concentrations of 100.0, 500.0, and 5,000.0 ng/mL in the samples. A 50 µL aliquot of the 1,000 ng/mL working internal standard solution was then added to each sample. Six samples at each concentration were analyzed, and the paraquat and diquat peak areas (C) were determined. A 95 µL aliquot of methanol was analyzed in the same way, and the corresponding peak area (D)

Table 1. Trueness and imprecision (n = 6).

Analyte	Standard addition concentration (ng/mL)	Mean ± SD (ng/mL)	Recovery (%)	CV (%)
Paraquat	274.51	260.75 ± 2.43	94.99 ± 0.88	0.93
	666.67	652.06 ± 11.05	97.81 ± 1.66	1.69
	5,078.43	5,316.87 ± 125.85	104.70 ± 2.48	2.37
Diquat	274.51	241.72 ± 3.49	88.06 ± 1.27	1.44
	666.67	625.26 ± 7.08	93.79 ± 1.06	1.13
	5,078.43	4,844.32 ± 128.27	95.39 ± 2.53	2.65

Table 2. Intraday and inter-day precision and accuracy of plasma paraquat and diquat concentration by HPLC-MS/MS (n = 6).

Analyte	Intraday			Inter-day		
	Mean ± SD (ng/mL)	Accuracy (%)	CV (%)	Measured value (ng/mL)	Accuracy (%)	CV (%)
Paraquat concentration (ng/mL)						
20	20.70 ± 0.52	103.50 ± 2.58	2.5	20.69 ± 0.54	103.43 ± 2.69	2.60
100	99.96 ± 2.75	99.96 ± 2.75	2.77	100.51 ± 3.32	100.51 ± 3.32	3.31
500	497.54 ± 7.85	99.51 ± 1.57	1.58	497.36 ± 7.69	99.47 ± 1.54	1.55
5,000	5,043.00 ± 142.64	100.86 ± 2.85	2.83	5,019.41 ± 164.20	100.39 ± 3.28	3.27
Diquat concentration (ng/mL)						
20	19.50 ± 0.86	97.35 ± 4.28	4.4	19.47 ± 1.20	97.00 ± 6.01	6.19
100	95.97 ± 3.95	97.65 ± 2.95	4.15	97.50 ± 4.43	96.39 ± 4.19	4.54
500	513.20 ± 17.90	102.82 ± 1.93	3.5	512.33 ± 15.74	102.47 ± 3.15	3.07
5,000	5,087.76 ± 121.12	100.22 ± 3.12	2.38	5,018.53 ± 174.39	100.37 ± 3.49	3.47

Table 3. Comparison of paraquat and diquat patient death group and survival group.

Paraquat					
Death group	51.71 ± 20.76	13 (8.0, 24.0)	71.50 (62.75, 126.25)	5,288.06 (2,311.94, 10,000.00)	60.00 (27.63, 80.00)
Survival group	42.64 ± 20.66	24 (8.0, 72.0)	61.50 (51.25, 66.00)	235.41 (50.19, 635.13)	4.54 (0.83, 10.99)
t	1.244	-0.968	-2.059	-5.340	-5.648
p	0.218 *	0.333 #	0.008 #	0.000 #	0.000 #
Diquat					
Death group	26.45 ± 10.72	10 (8, 23.25)	162.00 (103.25, 239.50)	9,087.10 (3,587.25, 10,000.00)	77.62 (52.64, 92.36)
Survival group	29.17 ± 13.49	12 (8, 24.00)	65.00 (56.00, 97.75)	248.74 (63.43, 878.21)	3.5 (1.22, 6.01)
t	1.031	-0.595	-4.926	-7.371	-7.650
p	0.883 *	0.552 #	0.000 #	0.000 #	0.000 #

Nonparametric rank sum test analysis results, * *t*-test analysis results.

Table 4. Area under the ROC curve for prognosis assessment of SIPP and SIDP, plasma concentration and serum creatinine.

Indicators	Area under ROC curve	Standard error	p	95% confidence		Youden index	Cutoff value
				upper bound	lower bound		
Paraquat							
SIPP	0.946	0.025	0.000	0.996	0.896	0.810	22.84 (h·mg)/L
Plasma paraquat concentration	0.919	0.034	0.000	0.986	0.852	0.733	1,087.84 (ng/mL)
Serum creatinine	0.710	0.074	0.008	0.856	0.565	0.419	66.50 (µmol/L)
Diquat							
SIDP	0.998	0.002	0.000	1.000	0.995	0.985	15.64 (h·mg)/L
Plasma diquat concentration	0.980	0.014	0.000	1.000	0.952	0.893	2,198.65 (ng/mL)
Serum creatinine	0.821	0.044	0.000	0.908	0.734	0.649	86.50 (µmol/L)

was determined. The absolute matrix effect was defined as the peak intensity for group C divided by the peak intensity for group D. The internal standard normalized matrix effect factor was defined as the absolute matrix effect of the test compound divided by the absolute matrix effect of the internal standard. The internal standard normalized matrix effect factors were markedly better than the absolute matrix effect factors, ranging 0.90 - 1.09. The serum matrix had a negligible effect on paraquat and diquat determination. The internal standard normalized matrix effect factors for paraquat QCs were 104.3%, 95.2%, and 99.01%, and for diquat QCs, they were 100.2%, 94.5%, and 94.1%.

Clinical validation

General information

Samples from 35 males and 27 females suffering paraquat poisoning, along with those from 40 males and 56 females suffering diquat poisoning, were analyzed. During the 30-day follow-up period, 42 deaths were caused by paraquat poisoning (mortality rate 67.7%) and 28 deaths were caused by diquat poisoning (mortality rate 29.2%). The paraquat or diquat concentrations and SIPPs were significantly higher for the death group than the survival group ($p < 0.05$), as shown in Tables 3 and 4.

Relationships between creatinine concentrations in serum, paraquat concentrations in plasma, SIPPs, and prognosis

The SIPP for the 62 patients with paraquat poisoning was 29.4 (h·mg)/L (8.7 - 72.3 (h·mg)/L). The prognostic value was stronger for the SIPP than the SCr and concentration in plasma. The SIPP for the death group was significantly higher ($p < 0.05$) than the SIPP for the survival group. The results are shown in detail in Tables 3 and 4 and Figure 2.

Relationships between the creatinine concentrations in serum, diquat concentrations in plasma, SIDP, and prognosis

The SIDP for the 96 patients with diquat poisoning was 5.28 (h·mg)/L (quartiles 1.56 and 38.7 (h·mg)/L). The prognostic value was stronger for the SIDP than the SCr and concentration in plasma. The SIDP for the death group was significantly higher ($p < 0.05$) than the SIDP for the survival group. The results are shown in detail in Tables 3 and 4 and Figure 3.

DISCUSSION

It has been found in routine clinical practice that discrepancies between reported and actual amounts of toxicants ingested can cause medical disputes. Such discrepancies can be caused by false recollections, post-ingestion vomiting, or poor herbicide regulations [18]. We determined the concentrations of paraquat and diquat in plasma and urine from the patients at admission so that the amounts of paraquat and diquat to which the patients were actually exposed could be estimated.

Paraquat and diquat are both very polar bipyridine compounds. Liquid chromatography is commonly used to determine such compounds in biological samples. However, traditional methods involve complex pretreatment steps such as liquid-liquid extraction, column switching, and solid-phase extraction, which are time-consuming and expensive [1,4,19]. We used a simpler and less time-consuming one-step protein precipitation (caused by adding methanol) method to prepare the samples because paraquat and diquat have low binding affinities for plasma proteins. Paraquat and diquat are suitable for positive electrospray ionization and are poorly retained by typical reverse-phase chromatographic columns. In a preliminary experiment, we used a C18 column with a mobile phase mixture of water containing

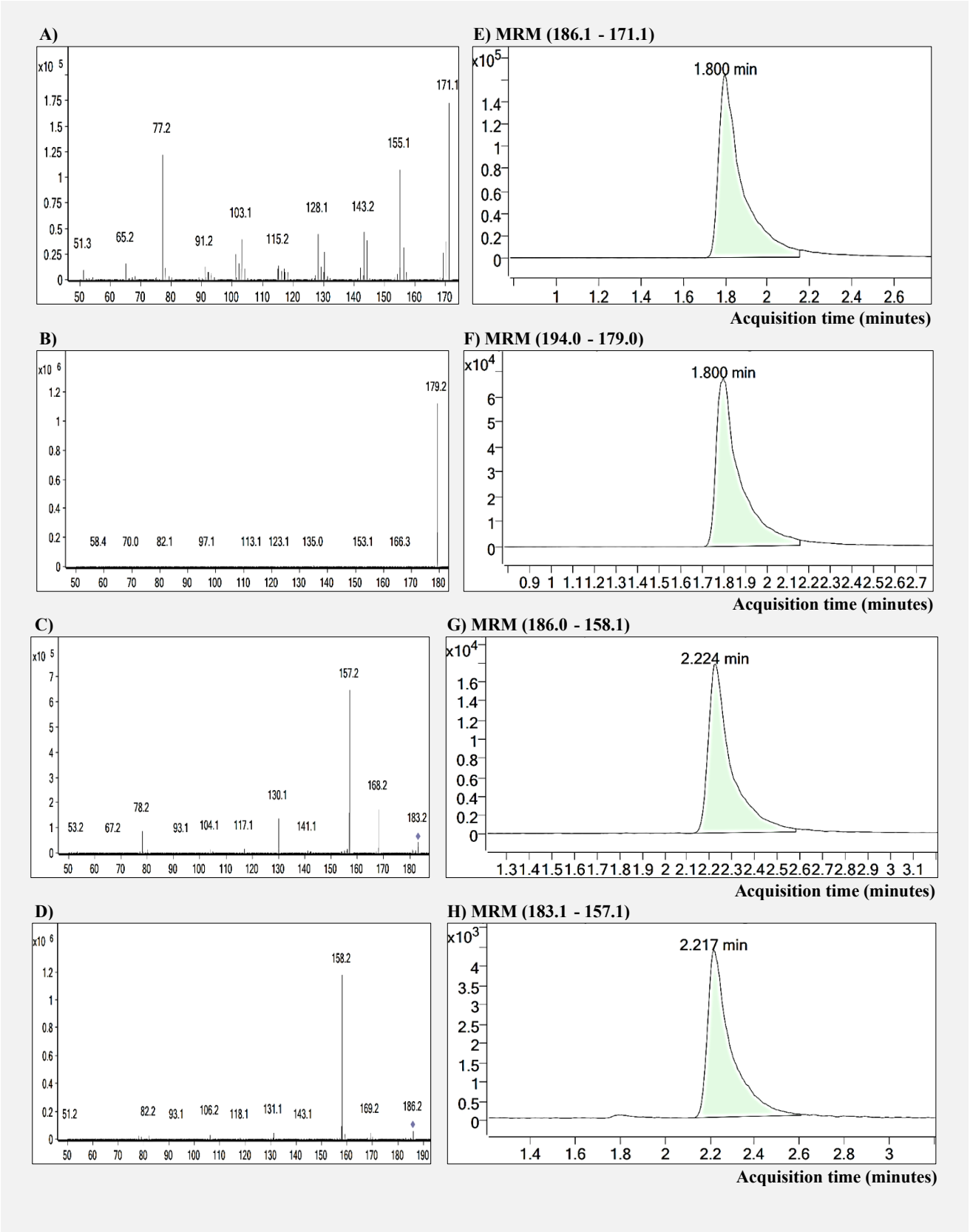

Figure 1. Product ion chromatograms for A) paraquat, B) paraquat-d8, C) diquat, and D) diquat-d4, and multiple reaction monitoring (MRM) chromatograms for analyte-free blood spiked with 500 ng/mL of standards and internal standards: E) paraquat, F) paraquat-d8, G) diquat, and H) diquat-d4.

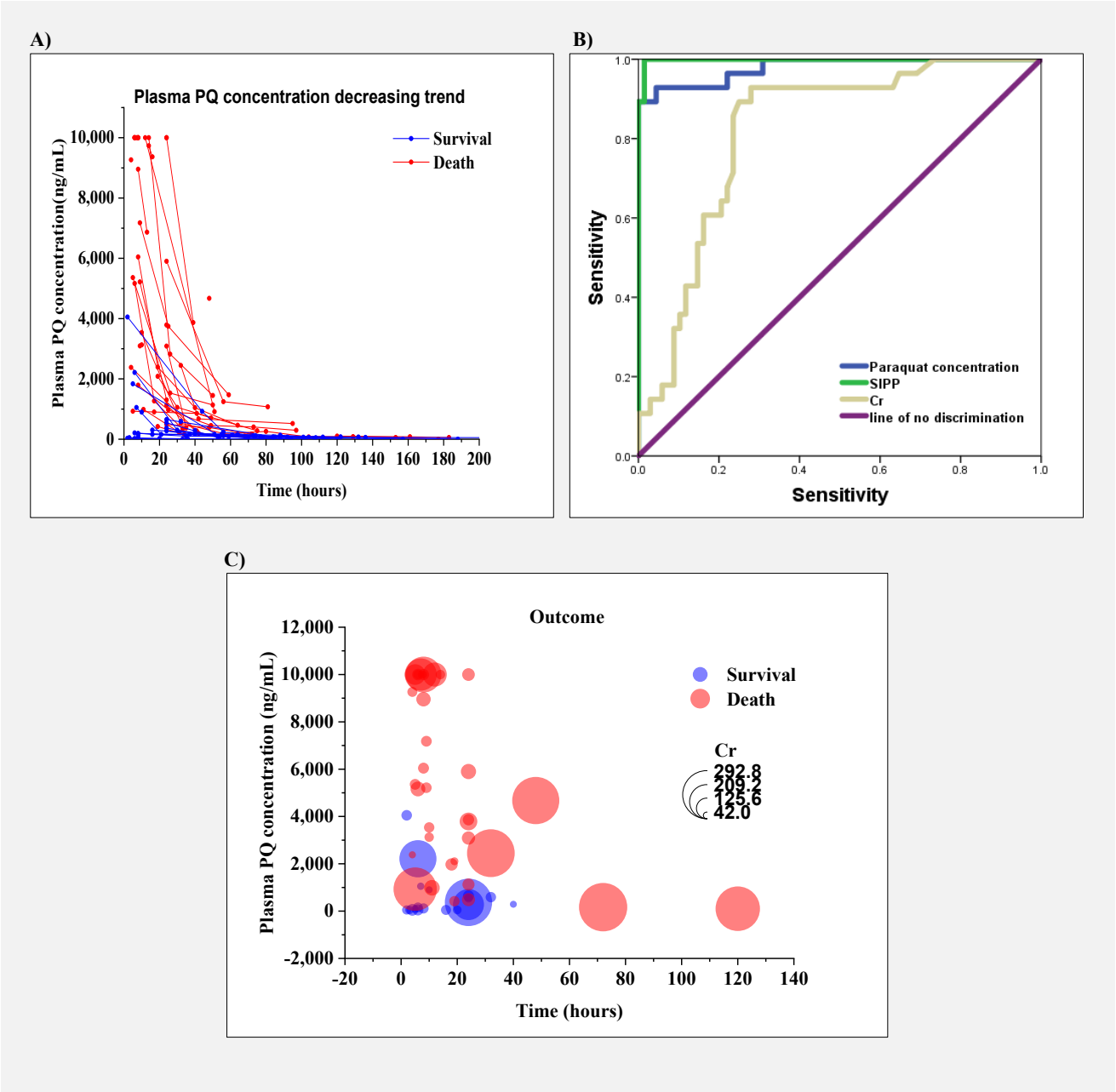

Figure 2. Paraquat (PQ) concentration in plasma decreasing over time A), receiver operating characteristic curves of evaluation indicators for paraquat poisoning B), relationship between the paraquat concentration in plasma on admission and prognosis C).

20 mmol/L ammonium formate and 0.1% formic acid A) and acetonitrile B). No paraquat, diquat, or internal standard peaks were found. A strongly-polar HILIC column was therefore used with a mobile phase with a high proportion of the organic phase to allow strongly-polar compounds to be retained. This enhanced the sensitivity of the electrospray ionization mass spectrometer and gave a strong ion response. Isocratic elution with a 60% water and 40% acetonitrile mobile phase caused paraquat and diquat to elute too early, meaning the responses were poor because of poor separation, poor peak shapes, and a low ionization efficiency. Gradient elution effectively separated the target compounds and gave good responses. This indicated the importance of using an appropriate mobile phase to the peak shape. The responses and peak shapes were poor when methanol or acetonitrile was used as the solvent, but using a proportion of water improved both the responses and peak shapes. Each sample was therefore injected into a 2:1 methanol:water mixture to ensure that the peak shape was satisfactory.

Plasma samples collected from poisoned patients when

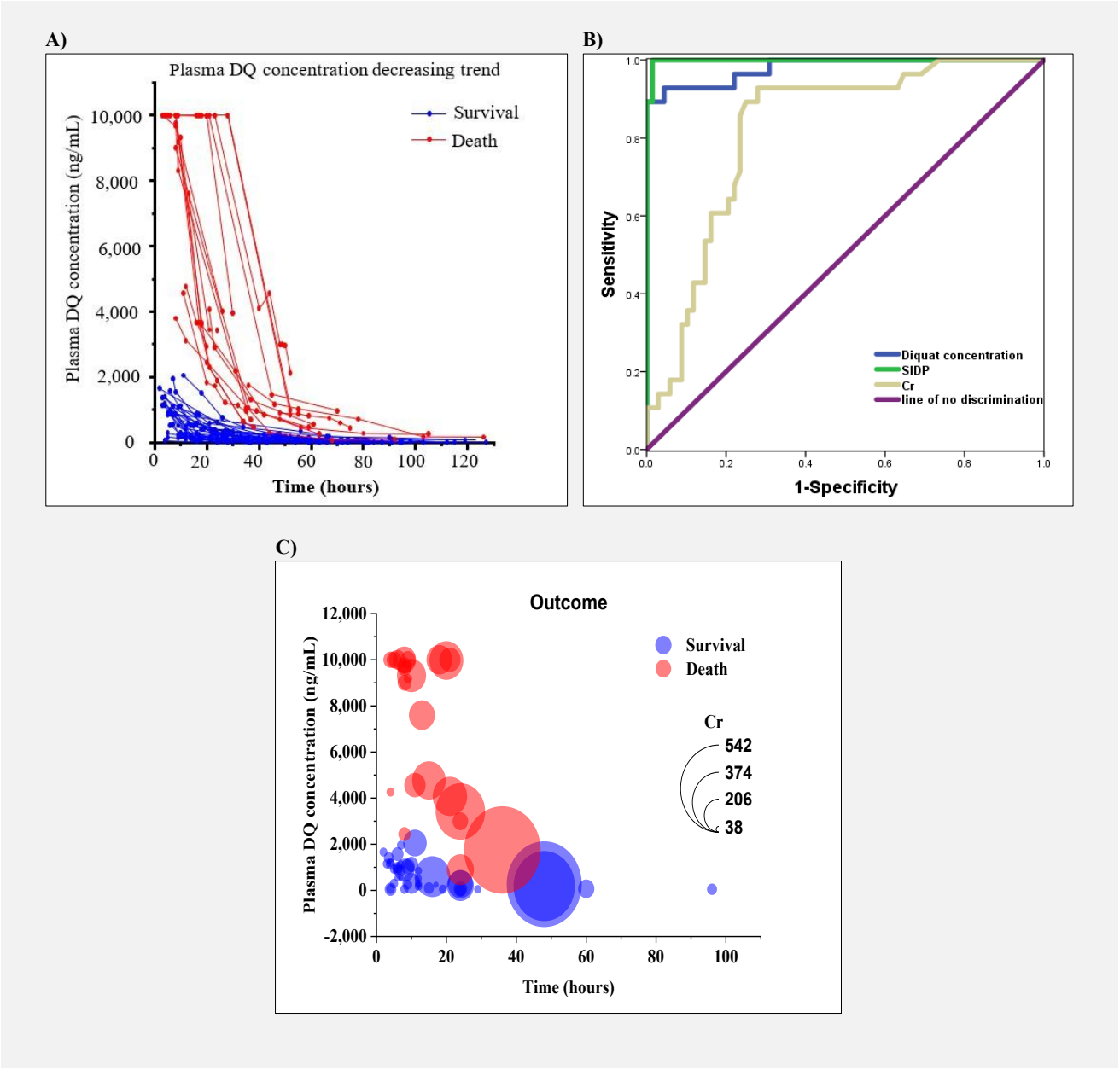

Figure 3. Diquat (DQ) concentration in plasma decreasing over time A), receiver operating characteristic curves of evaluation indicators for diquat poisoning B), relationship between diquat concentration in plasma on admission and prognosis C).

they were admitted to hospital between March 2017 and February 2024 were analyzed. Samples from 158 patients were analyzed, and at least one sample per patient was analyzed. Samples from 72 patients were collected and analyzed more than three times, and the paraquat and diquat concentrations in plasma were found to be slightly lower after than before irrigation. However, there were also exceptional cases. The paraquat and diquat concentrations varied between irrigations because irrigation would have caused the herbicides to be released to the blood from tissues containing high herbicide concentrations. Paraquat reaches higher concentrations in the lungs and skeletal muscle tissues than other tissues, with the concentration being highest (10 - 90 times higher than the concentration in plasma) in the lungs [17]. In contrast, diquat reaches higher concentrations in the liver and kidneys than in other tissues [20, 21]. Paraquat and diquat can be excreted in urine, and concentrations in urine can frequently be detected, but it is difficult to monitor paraquat or diquat concentrations in urine because the concentrations are not always detectable. Acute kidney injury caused by paraquat or diquat often manifests as oliguria or anuria, which can prevent continual assessment of paraquat or diquat con-

centrations in urine. The paraquat and diquat concentrations in plasma that we determined indicated that the paraquat and diquat severity indices could be used as valuable prognostic markers.

Paraquat poisoning prognoses for patients can be divided by the SIPP into mild (SIPP < 10), moderate (10 ≤ SIPP ≤ 50), and severe (SIPP > 50) [22-24]. Diquat poisoning prognoses based on the amount consumed can be divided into mild (< 1 g), moderate to severe (1 - 12 g), and fulminant (> 12 g) [25]. It is difficult to assess diquat consumption, but the SIDP can help correlate the diquat concentration in plasma with time since exposure. There are no specific antidotes for paraquat and diquat, so early prognosis of paraquat and diquat poisoning is crucial to guide treatment and improve clinical communication to prevent disputes and wasting of resources.

CONCLUSION

A reliable high-performance liquid chromatography tandem mass spectrometry method for determining paraquat and diquat in plasma easily, quickly, and sensitively was developed and was found to be suitable for clinical testing. Positive correlations were found between mortality rate and the SIPP and SIDP. However, the best measure for preventing paraquat and diquat poisoning remains public education about the dangers of paraquat and diquat.

Source of Funds:
This study was supported by National Key Technologies R&D Program provided by Ministry of Science and Technology of the People's Republic of China (project grant: 2022YFC3602300, sub-project grant: 2022YFC3602301). The three authors had unrestricted access to the research data and take responsibility for the submission for publication.

Ethical Approval Statement:
The study was approved (approval number IIT2023038 3B-R1) by the Clinical Research Ethics Committee of the First Affiliated Hospital, School of Medicine, Zhejiang University. Written informed consent was waived by the Institutional Review Board. The principles of the Helsinki Declaration guided the treatment protocol.

Declaration of Interest:
The authors state no conflict of interest.

References:

1. Fuke C, Ameno K, Ameno S, Kinoshita H, Ijiri I. Detection of two metabolites of diquat in urine and serum of poisoned patients after ingestion of a combined herbicide of paraquat and diquat. Arch Toxicol 1996;70(8):504-7. (PMID: 8783814)

2. Tan JT, Letchuman Ramanathan G, Choy MP, Leela R, Lim BK. Paraquat poisoning: experience in hospital taiping (year 2008 - october 2011). Med J Malaysia 2013;68(5):384-8. (PMID: 24632866)

3. Wunnapuk K, Mohammed F, Gawarammana I, et al. Prediction of paraquat exposure and toxicity in clinically ill poisoned patients: a model based approach. Br J Clin Pharmacol 2014;78(4):855-66. (PMID: 24697850)

4. Mao Z, Yu Y, Sun H, et al. Development and validation of a sensitive and high throughput UPLC–MS/MS method for determination of paraquat and diquat in human plasma and urine: application to poisoning cases at emergency departments of hospitals. Forensic Toxicol 2021;40(1):102-10. (PMID: 36454496)

5. Rose MS, Smith LL, Wyatt I. Evidence for energy-dependent accumulation of paraquat into rat lung. Nature 1974; 252(5481):314-5. (PMID: 4431454)

6. Charles JM, Aboudonia MB, Menzel DB. Absorption of paraquat and diquat from the airways of the perfused rat lung. Toxicology 1978;9(1-2):59-67. (PMID: 653742)

7. Zhou JN, Lu YQ. Lethal diquat poisoning manifests as acute central nervous system injury and circulatory failure: A retrospective cohort study of 50 cases. EClinicalMedicine 2022; 52(101609-20. (PMID: 35990582)

8. Vu AP, Nguyen TN, Do TT, et al. Clinical screening of paraquat in plasma samples using capillary electrophoresis with contactless conductivity detection: Towards rapid diagnosis and therapeutic treatment of acute paraquat poisoning in Vietnam. J Chromatogr B Analyt Technol Biomed Life Sci 2017;1060(111-7. (PMID: 28609698)

9. Maya F, Manuel Estela J, Cerda V. Improved spectrophotometric determination of paraquat in drinking waters exploiting a Multisyringe liquid core waveguide system. Talanta 2011;85(1):588-95. (PMID: 21645746)

10. Sha O, Cui B, Chen X, et al. Separation and Determination of Paraquat and Diquat in Human Plasma and Urine by Magnetic Dispersive Solid Phase Extraction Coupled with High-Performance Liquid Chromatography. J Anal Methods Chem 2020;2020(7359582-95. (PMID: 32724702)

11. Ghavidel F, Shahtaheri SJ, Torabbeigi M, Froushani AR. Optimization of solid phase microextraction procedure for determination of paraquat using reduction process. J Anal Chem 2016;71(7):648-52. https://link.springer.com/10.1134/s106193481607008x

12. Mao Z, Yu Y, Sun H, et al. Simultaneous determination of diquat and its two primary metabolites in rat plasma by ultra-performance liquid chromatography-tandem mass spectrometry and its application to the toxicokinetic study. Forensic Toxicol 2022;40(2):332-9. (PMID: 36454415)

13. Guo H, Li L, Gao L. Paraquat and Diquat: Recent Updates on Their Pretreatment and Analysis Methods since 2010 in Biological Samples. Molecules 2023;28(2):684-703. (PMID: 36677742)

14. Gao J, Feng SY, Wang J, Yang SY, Li Y. Prolonged methylprednisolone therapy after the pulse treatment for patients with moderate-to-severe paraquat poisoning A retrospective analysis. Medicine 2017;96(25):7244-8. (PMID: 28640126)

15. Williams PF, Jarvie DR, Whitehead AP. Diquat Intoxication: Treatment by Charcoal Haemoperfusion and Description of a New Method of Diquat Measurement in Plasma. J Toxicol Clin Toxicol 1986;24(1):11-20. (PMID: 3701905)

16. Qian W, Xie X, Zhou J, et al. Construction of a risk prediction model of diquat poisoning based on clinical indicators. Crit Rev Toxicol 2025;55(1):55-62. (PMID: 39688342)

17. Zhang Y, Chen X, Du H, Zhao M, Jiang X. Association between initial diquat plasma concentration, severity index and in-hospital mortality in patients with acute diquat poisoning: a retrospective cohort study. Clin Toxicol (Phila) 2024;62(9): 557-63. (PMID: 39222074)

18. Yuan G, Li R, Zhao Q, et al. Simultaneous determination of paraquat and diquat in human plasma by HPLC-DAD: Its application in acute poisoning patients induced by these two herbicides. J Clin Lab Anal 2021;35(3):329-32. (PMID: 33296104)

19. Ruan X-L, Qiu J-J, Wu C, et al. Magnetic single-walled carbon nanotubes-dispersive solid-phase extraction method combined with liquid chromatography-tandem mass spectrometry for the determination of paraquat in urine. J Chromatogr B Analyt Technol in the Biomed Life Sci 2014; 965(1):85-90. (PMID: 24999616)

20. Yu G, Jian T, Cui S, et al. Acute diquat poisoning resulting in toxic encephalopathy: a report of three cases. Clin Toxicol (Phila) 2022;31(2):647-50. (PMID: 34982016)

21. Huang Y, Zhang R, Meng M, Chen D, Deng Y. High-dose diquat poisoning: a case report. J Int Med Res 2021;49(6):1-10. (PMID: 34182818)

22. Xu SY, Hu H, Jiang Z, et al. APACHE Score, Severity Index of Paraquat Poisoning, and Serum Lactic Acid Concentration in the Prognosis of Paraquat Poisoning of Chinese Patients. Pediatr Emerg Care 2015;31(2):117-21. (PMID: 25654678)

23. Tang G, Jiang Z, Xu L, et al. Development and validation of a prognostic nomogram for predicting in-hospital mortality of patients with acute paraquat poisoning. Sci Rep 2024; 14(1):1622-32. (PMID: 38238454)

24. Hart TB NA, Whitehead A. A new statistical approach to the prognostic significance of plasma paraquat concentrations. Lancet 1984 2((8413)):1222-3. (PMID: 6150271)

25. Jones GM, Vale, J. A. Mechanisms of Toxicity, Clinical Features, and Management of Diquat Poisoning: A Review. Clin Toxicol (Phila) 2000; 38(123-8. (PMID: 10778908)