Science and Technology Indonesia
e-ISSN:2580-4391 *p*-ISSN:2580-4405
Vol. 9, No. 3, July 2024

Research Paper

Validated Chromatography Method for Analysis of Formaldehyde Migration Levels in Bottled Drinking Water

Nur Ramadhani[1,3]*, Risfah Yulianty[2], Yusnita Rifai[2], Muhammad Aswad[2], Gemini Alam[2], Tadjuddin Naid[2], Athia Kurnia Kasim[1]

[1] *Faculty of Pharmacy, Hasanuddin University, Makassar, South Sulawesi, 90245, Indonesia*
[2] *Departement of Pharmacy Science dan Technology, Faculty of Pharmacy, Hasanuddin University, Makassar, South Sulawesi, 90245, Indonesia*
[3] *Academy of Pharmacy Bina Pharmacy, Central Sulawesi, 94224, Indonesia*
***Corresponding author**: ramadhani.nur08@gmail.com

Abstract

Polyethylene terephthalate (PET) is utilized in the containment of potable water, nonetheless, it is susceptible to impairment due to temperature and duration of storage. Migration of formaldehyde from PET arises as a consequence of thermal deterioration. This study aims to ascertain the extent of formaldehyde transference in PET-contained drinking water of varying condition, subjected to diverse temperature setting and storage durations. An examination into the levels of formaldehyde migration in polyethylene terephthalate (PET) bottled drinking water was effectively carried out employing a validated high-performance liquid chromatography (HPLC) technique. A total of 162 water samples from three different PET bottled water brands sourced from supermarkets in Palu City, Central Sulawesi, Indonesia, underwent analysis. The formaldehyde assessment was executed utilizing a mobile phase composition of methanol:acetonitrile:water (48:12:40 v/v) for 12.97 minutes at a flow rate of 0.8 mL/minute on the 1st day, the 14th day, and the 42nd day while stored at room temperature and exposed to sunlight. Formaldehyde, lacking effective chromophoric entities and not readily ionizable, necessitated derivatization with 2,4-dinitrophenylhydrazine before HPLC analysis. The findings of the study demonstrated exceptional method linearity within the concentration span of 0.5 to 1321 μg/mL, exhibiting a commendable correlation coefficient of 0.999. The limit of detection (LOD) and quantification (LOQ) were determined to be 17.33 and 57.76 μg/mL, correspondingly. Precision evaluations displayed average intraday and interday values of 128.46±3.48% and 103.19±0.12%, respectively (%RSD < 2/3 CV Horwitz ratio). The intraday and interday %recovery values were computed at 97.22±3.48% and 96.83±0.14% ($n = 6$). The scrutiny of formaldehyde concentrations in the water samples unveiled the absence of formaldehyde migration.

Keywords

Bottled Drinking Water, Formaldehyde, Polyethylene Terephthalate, Validation

Received: 29 March 2024, Accepted: 21 May 2024
https://doi.org/10.26554/sti.2024.9.3.660-668

1. INTRODUCTION

The utilization of plastic prevails within the bottled drinking water industry sector. Polyethylene terephthalate (PET), a type of plastic utilized as a packaging material, has garnered significant attention due to its malleability and ability to withstand high temperatures (approximately 220°C) (Ikhsan et al., 2022; Tsaridou and Karabelas, 2021).

Nonetheless, PET material has been identified to harbor various small oligomers with low molecular weight, and the presence of aldehyde compounds has been detected (Alamri et al., 2021). Among these compounds, formaldehyde, a substance capable of dissolving in water and formed during the PET manufacturing process, is responsible for the existence of formaldehyde residues in food and beverage items (Ambadekar et al., 2020; Fappiano et al., 2022; Gerassimidou et al., 2022). Formaldehyde is generated through the polymerization reaction and the melting procedure in the manufacturing of PET bottles. The formation of carboxyl and vinyl ester chain terminations arises from the cleavage of polymer chain bonds. Formaldehyde is produced by the internal rupture of the polymeric chain (Abdelhakim et al., 2023).

Studies investigating the concentrations of formaldehyde present in the drinking water of various countries including Italy, Iran, Japan, Canada, Cairo, and Taiwan have revealed the phenomenon of formaldehyde migration within these water sources. The levels of formaldehyde in Tanzania and Poland, on the other hand, are subject to fluctuations based on factors such as temperature and duration of storage (Abdelhakim et al., 2023; Abe et al., 2021; Dehghani et al., 2018; Lugwisha et al., 2016).

Formaldehyde (CH_2O) is a chemical compound that permeates into potable water and exhibits toxicity, consequently being designated as a Group I carcinogen by the International Agency for Research on Cancer (IARC) (Abdelhakim et al., 2023; Cincotta et al., 2018; Protano et al., 2022; European Commission, 2011). Migration limits are a crucial aspect of the chemical criteria necessary for upholding the quality of bottled drinking water, thus safeguarding the consumers' safety and well-being. Bottled water products are mandated to adhere to migration limit specifications, set at 15 mg/kg by the World Health Organization or 900 μg/L by the Ministry of Health of Indonesia, prior to their distribution, in addition to meeting the Indonesian National Standards (Tsaridou and Karabelas, 2021; European Commission, 2011; World Health Organization, 2005; Minister of Industry of the Republic of Indonesia, 2016).

Formaldehyde arises as a result of the cleavage of polymer chain bonds within PET. The reversible binding of formaldehyde to the polymer system facilitates its effortless dissolution into potable water. The diffusion of formaldehyde persists until it attains equilibrium. Formaldehyde originates from the degradation of polymer chain bonds in PET, participating in a reversible bonding with the polymer matrix to facilitate its distribution into drinkable water. The transport of formaldehyde continues until it reaches a point of balance. The level of formaldehyde contamination stemming from PET vessels depends on factors like storage temperature, storage period, and sunlight exposure (Abdelhakim et al., 2023).

Numerous investigations examining the quantification of formaldehyde levels in beverage products have employed diverse methodologies. These methodologies encompass a blend of solid-phase microextraction headspace (HS-SPME) and gas chromatography-mass spectrometry (GC-MS), a fusion of liquid chromatography-mass spectrometry, high-performance liquid chromatography with reversed-phase (RP-HPLC), high-performance liquid chromatography with evaporative light scattering detector (HPLC-ELSD), high-performance liquid chromatography-ultraviolet (HPLC-UV), a synthesis of ultra-fast liquid chromatography-mass spectrometry (UFLC-MS), and high-performance liquid chromatography with derivatization (Abe et al., 2021; Lugwisha et al., 2016; Cincotta et al., 2018; Hossain et al., 2016; Marcela et al., 2021; Sebaei et al., 2018; Yoshikawa et al., 2018).

A derivatization step is required for the direct determination of formaldehyde in bottled drinking water. In contemporary times, the employment of DNPH in derivatized methods remains prominent. Due to the high reactivity, low molecular mass, and absence of a strong chromophore in formaldehyde, derivatization is deemed necessary (Jin et al., 2021).

HPLC has emerged as a proficient method for the separation and quantification of compounds within complex mixtures under suitable calibration conditions, offering cost-effectiveness and simplicity. The choice of the derivatized high-performance liquid chromatography technique was made due to its inherent simplicity in comparison to alternative contemporary methodologies. This method is capable of identifying analytes that lack effective chromophoric functionalities and are not readily ionizable. Furthermore, it is substantiated by prior scholarly works that offer a comprehensive insight into formaldehyde compounds and can be executed following the standardized protocol outlined by the U.S. Environmental Protection Agency (EPA, 1992) for the Determination of Carbonyl Compounds in Drinking Water (Abdu Hussen, 2022; Faria et al., 2022; Moldoveanu and David, 2022; U.S. Environmental Protection Agency, 1992).

The aim of this research was to evaluate the correlation between the formaldehyde migration levels in PET bottled water and three distinct volume changes when exposed to various environmental conditions such as room temperature, sunlight exposure temperature, and different storage periods (1, 14, and 42 days). This study employed validated HPLC methodologies to ensure the precision, accuracy, reproducibility, and effectiveness of the investigation. Critical factors taken into account comprised system suitability (SST), sensitivity, linearity, precision, accuracy, detection limit, limit of quantification, and robustness.

2. EXPERIMENTAL SECTION

2.1 Materials

The materials used in the study include were HCHO (Merck), CH_3OH (Merck), CH_3CN (Supelco), 2,4-DNPH (Sigma-Aldri ch), water drinking samples A, B, and C (from Palu, Indonesia). The equipment used consists of a Shimadzu Prominence HPLC System with SPD-M20A DAD with automatic chromatographic peak integration (Column C_{18}, 250 mm × 4.6 mm, UV detector at 360 nm), pH meter (Metrohm), thermometer (Humidity), 0.45 μm syringe filter (Sartorius), orbital shaker (Heidolph), sonicator (Branson), and Waters Sep-Pak® C_{18} Cartridge WAT043345.

2.2 Procedure

2.2.1 Sample Preparation

Water drinking samples consist of three different brands with three volume variations: 330 mL, 600 mL, and 5000-6000 mL. Water drinking samples were randomly selected from available product batches. The production dates for each brand are nearly identical, and each water drinking sample has a shelf life of one year before the expiration date. Each water drinking sample was stored at room temperature (19-25°C) and exposed to sunlight (26-38°C). Subsequently, the water drinking samples were tested on days 1, 14, and 42 using a validated HPLC method.

2.2.2 Validation Method

The validation method in this research is based on the ICH Q2(R1) guidelines, with parameters including system suitability (SST), sensitivity, linearity, precision, accuracy, detection limit, limit of quantification, and robustness.

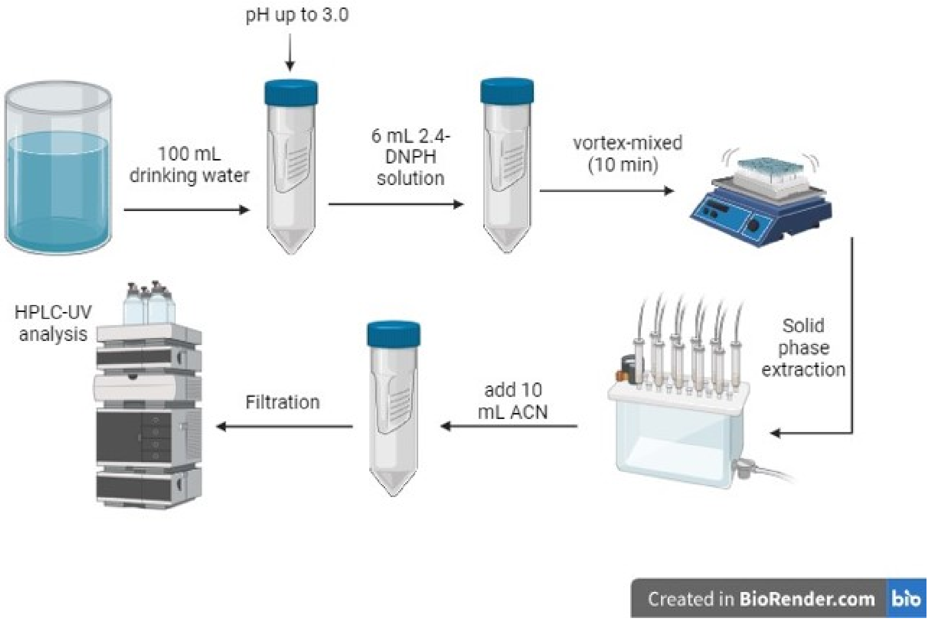

Figure 1. Schematic Representation of Water Drinking Samples Treatment

2.2.3 SST

SST was determined from six replicate injections of a formaldehyde standard solution with an injection volume of 40 μL over 12.57 minutes at a wavelength of 360 nm. The %RSD values for retention time, peak area, and tailing factor were then calculated. The acceptance criterion for %RSD is ≤ 2.7%.

2.2.4 Specificity Test

The specificity of the method was tested by injecting 40 μL each of a blank formaldehyde standard solution, 2,4-DNPH reagent blank and the water drinking sample into HPLC under the appropriate analysis conditions. Retention time and peak area were observed.

2.2.5 Linearity Test

For each concentration (0,5; 1; 1,5; 2; 2,5; 5,5; 11; 22; 44; 66; 110; 220; 440 and 1321 μg/mL), 40 μL was analyzed using HPLC with a mobile phase of methanol:acetonitrile:water (48:12:40, v/v), a flow rate of 0.8 mL/minute, a column temperature of 25°C, and formaldehyde concentration measured at a wavelength of 360 nm. The calibration curve was obtained using the linear regression equation of the formaldehyde-DNPH peak area versus concentration.

2.2.6 Precision and Accuracy Test

The precision and accuracy were evaluated using a standard addition method. One gram of water drinking sample was weighed, and 0.03 mL of a standard solution was added. The mixture was then injected as 32 μL into HPLC. Intra-day precision and accuracy were obtained from measurements on the same day, while inter-day precision and accuracy were obtained from replicated measurements on different days. The %RSD (for precision) and % recovery (for accuracy) were calculated, along with the 2/3 CV Horwitz value.

2.2.7 Detection Limit (LOD) and Quantification Limit (LOQ)

The LOD and LOQ values for both the instrument and method were calculated based on the standard deviation of the slope obtained from the linearity test.

2.2.8 Robustness Test

The robustness of the method was tested by measuring a 40 μL solution of formaldehyde 50 μL after applying slight changes to the analytical method. The flow rate was adjusted to 0.6 and 1.0 mL/minute, and the percentage of the mobile phase (methanol:acetonitrile:water) was changed to 38:15:47 v/v and 58:9:33 v/v. The robustness test was conducted on two different days.

2.2.9 Determination of Formaldehyde Migration Levels

Fill an Erlenmeyer flask with 100 mL of each drinking water sample. Perform derivatization in an acidic environment (pH=3) by adding 6 M HCl or 1 M NaOH. Next, add 6 mL of 2,4-DNPH solution. Cover every sample of drinking water right away, and then put the mixture in the sonicator set to 70°C for ten minutes. Saturated sodium chloride (10 ml) should be added to the derivatization solution. Proceed with solid phase extraction (SPE) by running 10 milliliters of pH 3 citrate buffer through the column to condition it. Quantitatively enter the solution in the column where the derivatization will take place. After derivatization, elute the solution with 8 milliliters of acetonitrile. Next, use acetonitrile to raise the volume to 10 mL. Analyze the solution to be derivatized using HPLC with a mobile phase of methanol:acetonitrile:water 48:12:40 v/v, flow rate 0.8 ml/min, column temperature 25°C and formaldehyde concentration measured at a wavelength of 360 nm. The scheme be seen in Figure 1. (Lugwisha et al., 2016; Hossain et al., 2016; Georgopoulou and Chrysikopoulos, 2018).

3. RESULTS AND DISCUSSIONS

This study uses a validated high-performance liquid chromatography (HPLC) method that had been derivatized with 2,4-DNPH to analyze the relationship between temperature and storage duration regarding the migration levels of formaldehyde in polyethylene terephthalate (PET) bottled drinking water with various volumes (Yoshikawa et al., 2018). The method is based on the standard U.S. Environmental Protection Agency (1992) for the Determination of Carbonyl Compounds in Drinking Water. Due to variations in the mobile phase and flow rate utilized, the HPLC analysis method required previous validation (Haque et al., 2021). This study took into account a number of factors, including as SST, sensitivity, linearity, precision, accuracy, detection limit, limit of quantification, and robustness (nternational Conference on Harmonisation of Technical Requirements For Registratation of Pharmaceuticals For Human Use, 2005).

The most crucial element in evaluating an HPLC technique validation is SST (Ravisankar et al., 2015). The percentage RSD values for tailing factor, peak area, and retention time in this investigation were 0.71±0.00, 6.48±0.71, and 3.21±0.78, respectively (Table 1). Values that show the integrity and dependability of the entire HPLC system during analysis and have a percentage RSD < 2.7% are accepted (Latimer Jr, 2016; Bose, 2014).

To make sure the study findings are accurate, the specificity test is carried out. The specificity test results show that during wavelength scanning, no additional analyte peaks were discovered during the formaldehyde peak's retention time. Using a standard formaldehyde solution with different concentrations 0.5, 1, 5, 5, 5, 11, 22, 44, 66, 110, 220, 440, and 1321 μg/mL, the absorbance of the solution was measured at 360 nm using the standard method in order to assess linearity (Singh et al., 2020). A linear regression equation, y=0.0254x+0.0525, with a correlation coefficient (r) of 0.9999 and a linear regression variance of 3.60%, was produced based on the absorbance values (Article et al., 2017). This suggests that the analysis technique can yield findings that closely match the formaldehyde levels in the drinking water sample (Rohyami and Pribadi, 2017). The developed calibration curve follows the Lambert-Beer rule, according to which the observed absorbance is exactly proportionate to the concentration. Increased sample concentrations are therefore correlated with increased absorbance levels (Hanin and Lestari, 2023). A formaldehyde standard chromatogram with a retention period of 3.233 mL/min is shown in Figure 3.

An analytical technique known as a precision test parameter quantifies the degree of agreement between a set of data obtained by repeat sampling the same drinking water sample under identical analysis circumstances. Two categories underwent precision testing in this investigation. Repetition by the same analyst on the same day and under the same analytical conditions was the first category, known as repeatability. Analyses conducted under identical analytical settings on various days were included in the second group, which was intermediate precision. The ICH recommendations state that measurements from 100% test concentration should be repeated at least six times (Ravisankar et al., 2015). The accuracy of the procedure was assessed using the values of the Horwitz ratio and the relative standard deviation (% RSD). According to the approval requirements, which were % RSD < 2/3 of the Horwitz ratio and repeatable precision with % RSD values ≤5.3%, the findings were fulfilled (Table 1) (Bose, 2014; Gnanavelu et al., 2021; Islam et al., 2021).

The degree to which the analysis findings closely match the actual analyte concentration is shown by the accuracy test parameter, which is an analytical process. Recovery as a percentage (%) is used to express accuracy. The simulation approach (spiked-placebo recovery) and the conventional addition method are the two ways to calculate accuracy (Rohyami and Pribadi, 2017). The standard addition method, which involves adding a certain quantity of standard solution to the water drinking sample in a defined amount, was employed in this investigation. In determining extremely low concentrations, this approach is thought to be more successful and to give high linearity (Sulistyaningrum et al., 2015; Chan et al., 2004). The process of recovery involved the addition of 0.03 mL of an internal standard solution.

Six duplicates of the spike analyses were performed on the water consumption sample. The ratio of the derived analyte concentration to the actual concentration is used to represent recovery. The results of the accuracy tests for this analytical approach ranged from 90.51 to 99.75% for intra-day recovery and from 95.82 to 96.18% for inter-day recovery (Table 1). Both the intra-day and inter-day percentage recovery are within the 90–107% acceptable range specified by the Association of Official Analytical Chemists (AOAC) (Bose, 2014; Setyaningsih et al., 2021). In addition, acceptable requirements were met by the percentage RSD values, which were determined to be less than 5.3% and less than two-thirds of the Horwitz ratio, respectively (Bose, 2014; Setyaningsih et al., 2021). Furthermore, percentage RSD values of less than 5.3% and percentage RSD less than two-thirds of the Horwitz ratio were found, both of which meet acceptability standards (Bose, 2014; Gnanavelu et al., 2021). The findings suggest that this testing method's high accuracy and appropriate percentage recovery requirements make it suitable for estimating the formaldehyde levels in bottled drinking water samples.

The limit of detection and limit of quantitation can be as-

Table 1. Method Validation Experimental Design and Result Summarys

Parameter	Experimental Design	Results
SST	Analysis of six replicate injections of a formaldehyde standard. Percentage RSD measurement for tailing factor, peak area, and retention duration.	• Duration of retention: – Average = 3.2055 – SD = 0.0248 – %RSD = 0.7750 • Peak area: – Average = 6.4822 – SD = 0.0463 – %RSD = 0.7174 • Tailing Factor: – Average = 0.8570 – SD = 0.0000 – %RSD = 0.0000
Specificity		No peak was found at the retention time of the appearance of formaldehyde and wavelength scanning.
Linearity	Analyzing the logarithmic calibration curve between 0.5 and 1321 µg/mL in terms of concentration.	• R = 0.9999 • Intercept = 0.0525 • Slope = 0.0254
Precision, Repeatability, Intermediate precision	Analysis of six homogeneous water drinking samples. Measurement of Mean±%RSD and 2/3 CV Horwitz value	• Mean±%RSD intraday = 128.4593±3.48 • 2/3 CV Horwitz = 5.14 • Mean±%RSD interday = 103.1890±0.12 • 2/3 CV Horwitz = 5.31
Accuracy	Addition of a known amount of standard solution to six replicate test water drinking samples.	• Mean±%RSD intraday = 97.2187±3.48 • 2/3 CV Horwitz = 5.36 • Mean±%RSD interday = 96.8334±0.14 • 2/3 CV Horwitz = 5.36
Limit of Detection Limit of Quantification		LOD = 17.3289 µg/mL LOQ = 57.7629 µg/mL
Robustness	Analysis of the impact of shifting the proportion of mobile phase and flow rate.	• Intraday: – Variation in flow rate 1.0 mL/min (%RPD = 2.21%) – Variation in flow rate 0.6 mL/min (%RPD = 1.72%) – Variation in the mobile phase MeOH: ACN: H_2O (38 : 15: 47) = 2.17% – Variation in the mobile phase MeOH: ACN: H_2O (58 : 9: 33) = 0.58% • Interday: – Variation in flow rate 1.0 mL/min (%RPD = 0.32%) – Variation in flow rate 0.6 mL/min (%RPD = 0.18%) – Variation in the mobile phase MeOH: ACN: H_2O (38 : 15 : 47) = 0.14% – Variation in the mobile phase MeOH: ACN: H_2O (58 : 9 : 33) = 0.19%

Table 2. Experimental Design and Summary of Results for Method Validation

Method	Matrix	Solvens; Derivatization Reagents	Run Time (min)	LOD (µg/mL)	Precision (%RSD)	Recovery	Reference
HPLC-UV	drinking water	DNPH; ACN	12.97	17.33	0.12-3.48	96.67-99.75	this work
LC-MS	drinking water	DNPH; ACN	20	not mentioned	2.6-3.9	82.00-103.6	(Marcela et al., 2021)
UFLC-MS	drinking water	DNPH; ACN	16.5	0.006 and 0.004	not mentioned	not mentioned	(Abe et al., 2021)

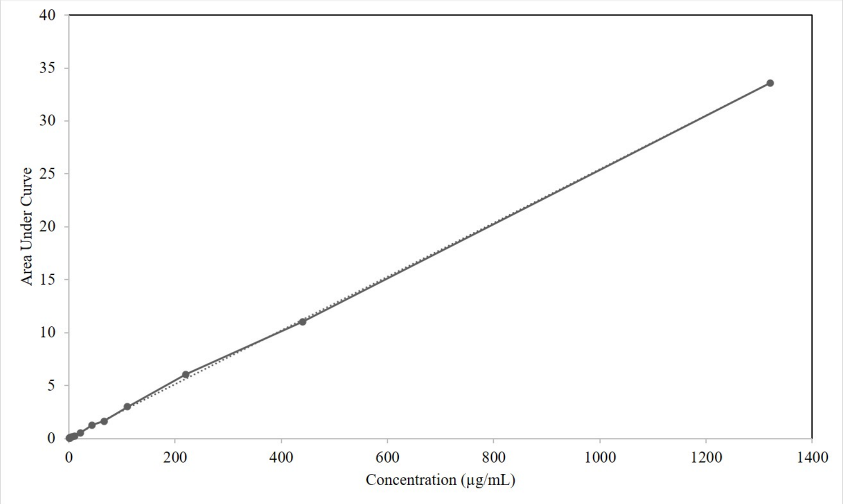

Figure 2. Calibration Curve of Formaldehyde Standard

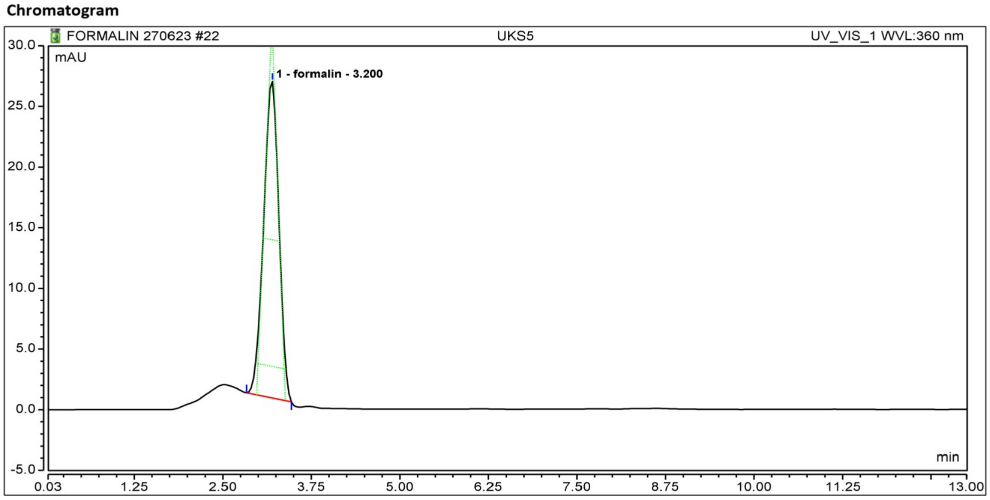

Figure 3. Chromatogram of Formaldehyde Standard

certained using the linearity test's standard deviation results. Common metrics used to evaluate the sensitivity of analytical techniques include LOD and LOQ. Lower LOD values showed stronger sensitivity, and the LOD indicated the method's sensitivity (Haque et al., 2021). The LOD and LOQ values of 17.33 and 57.76 μg/mL, respectively, show the level of sensitivity.

The robustness test parameter is an analytical technique that assesses a method's capacity to show consistently good performance under typical circumstances and to withstand even minor modifications to purposefully introduced method variations. This shows that it was appropriate and dependable for the analysis. The analytical approach uses several mobile phase ratios and flow rates in the resistance test. The relative percentage difference (% RPD) is a way to express the concentration variability of the analysis results. According to the National Standardization Agency (2018) and the U.S. Environmental Protection Agency, the requirements for this fall within the range of < 10%. When comparing the results of measuring the applied technique modifications to the precision of two measurements (duplicates) of water drinking samples taken under normal circumstances, RPD is displayed. Study findings indicate that RPD levels are less than 5%. There is no discernible difference in the RPD scores between intra- and inter-day testing. These findings indicate that the formaldehyde migration level may be determined with good resistance using this approach. Table 1 displays the results' verification.

In order to contextualize our analytical approach, it was juxtaposed with previously published drinking water methods (Table 2). Analysis time and two analytical figures of merit (LOD and recovery) were emphasized. However, LOD was more than that of any prior formaldehyde measurement technique used in drinking water, even when large sensivity techniques like LC-MS or UFLC-MS were used. The figures observed in earlier investigations ranged greatly in terms of recovery (82.00 to 103.6%).

3.1 Determination of Formaldehyde Migration Levels in Samples

HPLC with automatic chromatographic peak integration system is a digital technology with a higher degree of complexity. In the era of industry 4.0, implementation of digital technology helps improve the quality control of food and drug products. Its has higher retention time accuracy on 90%, peak start/end time on 0.2 minute to 1 minute, root-mean-square error on 0.4 minutes to 1.3 minutes, the application of this technology can produce more accurate and effective analytical results (Satwekar et al., 2023).

Our study aims to investigation of migration levels of formal

dehyde on the effect of photo-degradation. Photo-degradation by UV radiation and temperature variation and during storage can the results in the formation of carboxyl end-groups. Formaldehyde compound is the carboxyl end-group in the polymer chain. This study, 162 water drinking samples were subjected to the sample treatment procedure above (Section 2.2.9), showed formaldehyde was not detected in each of the water drinking samples. Migration level of formaldehyde < LOQ. The degradation of PET bottle has not occurred under sunlight or during storage, but rather the accumulation of carboxyl group during bottle processing and employing high temperatures during that. Previous research showed that formaldehyde migration levels were only seen on day 267 at 5.15 μg/mL. However, some studies show that formaldehyde migration levels can decrease on storage time due to degradation by heterotropic bacteria in the bottle under sunlight exposure on storage time (Abdelhakim et al., 2023). Formldehyde can cause organoleptical changes, however, in general, formaldehyde migration levels are still within the migration limit range.

The DAD detector of our instrument has limitations, namely the identification of compounds based only on retention time and UV spectra, as well as low detection limits and robustness in complex samples (López-Fernández et al., 2020). For this reason, it is necessary to change the samples in concentrate form and further study using liquid chromatography-Tandem mass spectrometry technique (LC-MS).

The undetected levels of formaldehyde migration in the packaged drinking water samples may be influenced by the increasing awareness and conscientiousness of manufacturers in controlling the production process of drinking water, particularly in the use of packaging materials, as well as the effective measures taken by the Indonesian Government regarding packaging and standardization of packaged drinking water.

4. CONCLUSIONS

The verified high-performance liquid chromatography method may be used to measure the amounts of formaldehyde migration in packaged drinking water, according to the research findings. In 162 PET-packaged drinking water samples that were being circulated in the Indonesian city of Palu, Central Sulawesi, formaldehyde migration was not found. Temperature (19 to 38°C) and stotage duration (one days, 14 days and 42 days) have little effect on the amount of formaldehyde that migrates at different volumes. This complies with the World Health Organization's (WHO) and the Ministry of Health's Decree Number 907/Menkes/SK/VII/2002 standards.

5. ACKNOWLEDGMENT

The author like to express my appreciation and special thanks to my advisors for their guidance and members my examination committee. Also, The authors like to express the gratitude to Academy of Pharmacy for funding this publication.

REFERENCES

Abdelhakim, A. A., M. S. Abdel-Aziz, and M. Sultan (2023). Migration of Acetaldehyde and Formaldehyde From Pet-Bottled Water Under Hot Climate Conditions. *Egyptian Journal of Chemistry*, **66**(11); 573–583

Abdu Hussen, A. (2022). High-Performance Liquid Chromatography (HPLC): A Review. *Annals of Advances in Chemistry*, **6**(1); 010–020

Abe, Y., N. Kobayashi, M. Yamaguchi, M. Mutsuga, A. Ozaki, E. Kishi, and K. Sato (2021). Determination of Formaldehyde and Acetaldehyde Levels in Poly(Ethylene Terephthalate) (Pet) Bottled Mineral Water Using A Simple and Rapid Analytical Method. *Food Chemistry*, **344**; 128708

Alamri, M. S., A. A. A. Qasem, A. A. Mohamed, S. Hussain, M. A. Ibraheem, G. Shamlan, H. A. Alqah, and A. S. Qasha (2021). Food Packaging's Materials: A Food Safety Perspective. *Saudi Journal of Biological Sciences*, **28**(8); 4490–4499

Ambadekar, S., D. Baburao Nikam, and S. Raju Ambadekar (2020). Formaldehyde in Baby Foods by HPLC-ELSD. *American Journal of Chemistry*, **2020**(2); 19–25

Article, O. R., Y. Vidushi, and B. Meenakshi (2017). A Review on HPLC Method Development and Validation. *Unnamed Journal*, **2**(166); 166–178

Bose, A. (2014). HPLC Calibration Process Parameters in Terms of System Suitability Test. *Austin Chromatography*, **1**(2); 1–4. Available from: www.austinpublishinggroup.com

Chan, C. C., H. Lam, Y. C. Lee, and N. Pharma (2004). *Analytical Method Validation and instrument Performance Verification*

Cincotta, F., A. Verzera, G. Tripodi, and C. Condurso (2018). Non intentionally Added Substances in Pet Bottled Mineral Water During the Shelf Life. *European Food Research and Technology*, **244**(3); 433–439

Dehghani, M. H., M. Farhang, and A. Zarei (2018). Investigation of Carbonyl Compounds (Acetaldehyde and Formaldehyde) in Bottled Waters in Iranian Markets. *International Food Research Journal*, **25**(2); 876–879

European Commission (2011). Commission Regulation (EU) No 10/2011 of 14 January 2011 on Plastic Materials and Articles Intended to Come into Contact with Food. *Official Journal of the European Union*, **12**; 1–89

Fappiano, L., F. Carriera, A. Iannone, I. Notardonato, and P. Avino (2022). A Review on Recent Sensing Methods For Determining Formaldehyde in Agri-Food Chain: A Comparison with the Conventional Analytical Approaches. *Foods*, **11**(9)

Faria, I. D. L., M. M. Gouvêa, A. D. Pereira Netto, and F. F. de Carvalho Marques (2022). Determination of Formaldehyde in Bovine Milk by Micellar Electrokinetic Chromatography with Diode Array Detection. *Lwt*, **163**

Georgopoulou, M. P. and C. V. Chrysikopoulos (2018). Evaluation of Carbon Nanotubes and Quartz Sand For the Removal of Formaldehyde- (2,4-Dinitrophenylhydrazine) From Aqueous Solutions. *Industrial & Engineering Chemistry Research*

Gerassimidou, S., P. Lanska, J. N. Hahladakis, E. Lovat, S. Vanzetto, B. Geueke, K. J. Groh, J. Muncke, M. Maffini, O. V. Martin, and E. Iacovidou (2022). Unpacking the Complexity of the Pet Drink Bottles Value Chain: A Chemicals Perspective. *Journal of Hazardous Materials*, **430**; 128410

Gnanavelu, A., T. S. Shanmuganathan, V. Deepesh, and S. Suresh (2021). Validation of A Modified Procedure For the Determination of Chemical Oxygen Demand Using Standard Dichromate Method in ndustrial Wastewater Samples with High Calcium Chloride Content

Hanin, N. and D. P. Lestari (2023). Determination of Nitrite in the Kapuas Besar River by Spectrophotometric Method. In *Proceeding International Conference on Religion, Sciences, and Education*, volume 2. pages 795–800

Haque, M. A., V. Bakshi, M. Thippani, R. M. Manda, and N. Boggula (2021). Development and Validation of UV Spectrophotometric Method For the Determination of Dolutegravir by Using Quality by Design (Qbd) Approach. *Journal of Advanced Scientific Research*, **12**(3). Available from: http://www.sciensage.info

Hossain, M. S., M. S. Islam, S. Bhadra, and A. S. Shamsur Rouf (2016). Investigation of Formaldehyde Content in Dairy Products Available in Bangladesh by A Validated High Performance Liquid Chromatographic Method. *Dhaka University Journal of Pharmaceutical Sciences*, **15**(2); 187–194

Ikhsan, A. N., M. C. Thohira, and D. Daniel (2022). Analysis of Packaged Drinking Water Use in Indonesia in the Last Decades: Trends, Socio-Economic Determinants, and Safety Aspect. *Water Policy*, **24**(8); 1287–1305

Islam, M. A., B. G. Jeong, W. L. Kerr, and J. Chun (2021). Validation of Phytosterol Analysis by Alkaline Hydrolysis and Trimethylsilyl Derivatization Coupled with Gas Chromatography For Rice Products. *Journal of Cereal Science*, **101**; 103305

Jin, X. C., R. M. Ballentine, W. P. Gardner, M. S. Melvin, Y. B. Pithawalla, K. A. Wagner, K. C. Avery, and M. Sharifi (2021). Determination of Formaldehyde Yields in E-Cigarette Aerosols: An Evaluation of the Efficiency of the DNPH Derivatization Method. *Separations*, **8**(9); 151

Latimer Jr, G. (2016). Guidelines for Standard Method Performance Requirements: Official Methods of Analysis. *AOAC International*; 1–18

López-Fernández, O., R. Domínguez, M. Pateiro, P. E. Munekata, G. Rocchetti, and J. M. Lorenzo (2020). Determination of Polyphenols Using Liquid Chromatography–Tandem Mass Spectrometry Technique (lC–MS/MS): A Review. *Antioxidants*, **9**(6); 479

Lugwisha, E., J. A. Mahugija, and C. Mwankuna (2016). Levels of Formaldehyde and Acetaldehyde in Selected Bottled Drinking Water Sold in Urban Areas in Tanzania. *Tanzania Journal of Science*, **42**(1); 1–14

Marcela, M. C. I., J. Pereira Dos Anjos, F. Oliveira Campos Da Rocha, and J. B. De andrade (2021). Exploratory Analysis of the Presence of 14 Carbonyl Compounds in Bottled Mineral Water in Polyethylene Terephthalate (Pet) Containers. *Food Chemistry*, **365**; 130475

Minister of Industry of the Republic of Indonesia (2016). Mandatory Implementation of the Indonesian National Standard for Mineral Water, Demineralized Water, Natural Mineral Water, and Dewatered Drinking Water. Indonesia

Moldoveanu, S. C. and V. David (2022). *Essentials in Modern HPLC Separations Second Edition*. Elsevier, Netherlands

nternational Conference on Harmonisation of Technical Requirements For Registratation of Pharmaceuticals For Human Use (2005). *Validation of Analytical Procedures: Text and Methodology Q2(R1)*. November 1996

Protano, C., G. Buomprisco, V. Cammalleri, R. N. Pocino, D. Marotta, S. Simonazzi, F. Cardoni, M. Petyx, S. Iavicoli, and M. Vitali (2022). the Carcinogenic Effects of Formaldehyde Occupational Exposure: A Systematic Review. *Cancers*, **14**(1)

Ravisankar, P., C. Naga Navya, D. Pravallika, and D. N. Sri (2015). A Review on Step-by-Step Analytical Method Validation. *IOSR Journal of Pharmacy*, **5**(10); 2250–3013

Rohyami, Y. and R. M. Pribadi (2017). Validation of Methods on Formalin Testing in Tofu and Determination of 3,5-Diacetyl-Dihydrolutidine Stability by UV-Vis Spectrophotometry. In *AIP Conference Proceedings*, volume 1911

Satwekar, A., A. Panda, P. Nandula, S. Sripada, R. Govindaraj, and M. Rossi (2023). Digital by Design Approach To Develop A Universal Deep Learning AI Architecture For Automatic Chromatographic Peak integration. *Biotechnology and Bioengineering*, **120**(7); 1822–1843

Sebaei, A. S., A. M. Gomaa, A. El-Zwahry, E. Emara, et al. (2018). Determination of Formaldehyde by HPLC with Stable Precolumn Derivatization in Egyptian Dairy Products. *International Journal of Analytical Chemistry*, **2018**; 1–5

Setyaningsih, D., Y. A. Santoso, Y. S. Hartini, Y. B. Murti, W. L. J. Hinrichs, and C. Patramurti (2021). Isocratic High-Performance Liquid Chromatography (HPLC) For Simultaneous Quantification of Curcumin and Piperine in A Microparticle Formulation Containing Curcuma Longa and Piper Nigrum. *Heliyon*, **7**(3); e06541

Singh, S., N. Sharma, N. Kanojia, G. Kaur, and S. Arora (2020). Development and Validation of UV-Spectrophotometer Method for Analysis of Fluvastatin Sodium in Polyethylene Glycol 6000 and Polyvinyl Pyrollidone K30 Solid Dispersions. *Plant Archives*, **20**(1); 3365–3371

Sulistyaningrum, I., M. P. G. Utami, R. B. Istiningrum, and I. M. Siregar (2015). Comparison Between the Calibration and the Standard Addition Methods in Determining Dissolved Lead in Borobudur's Control Tanks Water by Flame Atomic Absorption Spectrophotometry (F-AAS). *Procedia Chemistry*, **17**; 70–74

Tsaridou, C. and A. J. Karabelas (2021). Drinking Water Standards and Their Implementation—A Critical Assessment. *Water*, **13**(20); 2918

U.S. Environmental Protection Agency (1992). *Method 554. Determination of Carbonyl Compounds in Drinking Water by Dinitrophenylhydrazine Derivatization and High Performance Liquid Chromatography, Rev. 1.0. Methods For the Determination of Organic Compounds in Drinking Water, Suppl. II.* U.S. Environmental Protection Agency, Cincinnati, OH

World Health Organization (2005). Mercury in Drinking-Water, Background Document For Development of WHO Guidelines For Drinking-Water Quality

Yoshikawa, K., Y. Oshima, A. inagaki, and A. Sakuragawa (2018). Determination of Formaldehyde in Water Samples by High-Performance Liquid Chromatography with Methyl Acetoacetate Derivatization. *Bulletin of Environmental Contamination and Toxicology*, **101**(5); 672–677