Heliyon 10 (2024) e27559

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

A Selective Gas Chromatography–Tandem Mass Spectrometry Method for Quantitation of Ethylene and Diethylene Glycol in Paediatric Syrups

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ARTICLE INFO

Keywords:
Glycols
Pharmaceutical analysis
Gas Chromatography–Tandem Mass Spectrometry
Pharmaceutical impurities
Contaminants

ABSTRACT

Ethylene Glycol (EG) and diethylene Glycol (DEG) are two contaminants known to cause various human health problems. These glycols might be present in drug syrups that are based on glycerol, sorbitol, or polyethylene glycol. In late 2022, several batches of cough, antipyretics, and antihistamine syrups were reported to contain toxic levels of EG and DEG in multiple countries; this incident concerned the World Health Organization (WHO). From an analytical perspective, several methods of glycols analysis in pharmaceuticals have been reported in the literature, with the majority being dedicated to raw material analysis. This study aims to develop a selective method capable of evaluating a wide range of paediatric syrups in order to assess the safety of commercially available paediatric syrups currently distributed in the local market. This research introduces a method for determining glycols utilizing gas chromatography-tandem mass spectrometry (GC–MS/MS), which offers significantly higher selectivity than conventional single quadrupole gas chromatography-mass spectrometry (GC–MS). The developed method meets the current International Council for Harmonisation (ICH) guidelines for validation. The absence of any interfering peaks in both the unspiked sample of promethazine syrup and the reference standard solutions proved the method's selectivity. Furthermore, 2,2,2-trichloroethanol was used as an internal standard, and a new GC–MS/MS method was developed to analyze it. The calibration curves for EG and DEG were linear within the selected concentration range of 1–10 μg/mL. The detection limit for both EG and DEG was 400 ng/mL, while the quantification limit was 1 μg/mL. Recovery values for both EG and DEG met the accuracy acceptance criterion. Thus, the developed method proved to be efficient and accurate for determining EG and DEG levels in suspected contaminated syrups.

1. Introduction

Glycols are aliphatic dihydric alcohols that contain two hydroxyl groups [1,2]. They are colorless, sweet-tasting liquids with a wide range of industrial applications, particularly as solvents and antifreeze agents [3,4]. In the pharmaceutical industry, ethylene glycol

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https://doi.org/10.1016/j.heliyon.2024.e27559
Received 7 November 2023; Received in revised form 29 February 2024; Accepted 1 March 2024
Available online 15 March 2024
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(EG) and diethylene glycol (DEG) are contaminants that can be found in syrups that are based on glycerol (GLY), sorbitol, or polyethylene glycol (PEG). GLY, sorbitol, and PEG are widely used as excipients in pharmaceutical syrups because they possess multiple functions; they act as solvents, humectants, antimicrobials, and preservatives [5]. Additionally, as parent compounds, DEG and EG are relatively nontoxic. However, the toxicities of these substances arise from their metabolites, which can result in severe morbidity and an increased risk of mortality [6]. Their toxic effects can manifest in a variety of symptoms, such as abdominal pain, vomiting, diarrhea, headache, altered mental state, inability to urinate, and acute kidney injury, which can be life-threatening. Throughout history, there have been numerous cases of mass poisoning caused by the consumption of pharmaceuticals contaminated with EG and DEG. For example, between 1937 and 2008, more than 600 people died in multiple countries, including the United States, South Africa, Spain, India, Nigeria, Bangladesh, Argentina, Haiti, and Panama [7–10]. By the end of 2022, the World Health Organization (WHO) had issued an alert regarding substandard cough, antipyretic, and antihistaminic syrups that had been distributed in Indonesia and Gambia. Subsequently, laboratory analysis confirmed the presence of toxic levels of EG and DEG in those products, which, by then, had resulted in serious injuries and, unfortunately, some fatalities [11,12].

Several analytical methods have been reported in the literature for the determination of glycols in pharmaceuticals. The methods outlined in the United States Pharmacopoeia (USP) [13,14] and the European Pharmacopoeia [15] for determining glycols in GLY and PEG are intended for raw materials, not finished products. High-performance liquid chromatography–tandem mass spectrometry (HPLC–MS/MS) was used to analyze DEG in contaminated pharmaceuticals during the Haiti mass poisoning outbreak that occurred in the mid-1990s [7]. The analysis of both EG and DEG can also be done using thin-layer chromatography (TLC), where rapid-screening TLC apparatus is used to ensure ease, reliability, and portability [16]. Additionally, fourier transform infrared (FTIR) and near-infrared (NIR) spectroscopic methods have been employed for DEG determination, which are viable, simple, cost-effective, rapid, and environmentally friendly. However, despite their advantages, their sensitivity is lower than that of other analytical methods, such as chromatographic methods [17]. The capillary gas chromatographic (GC) method with flame-ionization detection has proven to be more sensitive and selective than FTIR spectroscopy, NIR spectroscopy, and TLC [18]. GC with single quadrupole mass spectrometry (GC/MS) or with triple quadrupole mass spectrometry (GC–MS/MS) allows for the separation of EG, DEG, and propylene glycol without the need for glycols derivatization or sample cleanup while demonstrating accurate and precise detection of glycols in pharmaceutical products. Furthermore, they can be used to assess the identity and content of EG and DEG in glycerin and glycerin-containing products [19]. These methods of analysis can also be easily automated, thereby improving efficiency, particularly when screening a large number of samples [18].

In this regard, detection in the multiple reaction monitoring (MRM) mode offers higher selectivity and less interference from the matrix because of the double mass filtering in the MRM mode compared to single ion monitoring (SIM) present in single quadrupole mass spectrometry [20]. The recent incident of glycol mass poisoning prompted us to evaluate the safety of the paediatric syrups currently distributed in the local market. The goal of this study was to develop and validate a selective method capable of determining EG and DEG in a wide range of commercial matrices using a triple quadrupole GC–MS/MS in a single run. To the best of our knowledge, this is the first time that such an investigation has been conducted in pharmaceutical analysis.

2. Materials and methods

2.1. Experimental analysis

2.1.1. Chemicals and reagents

EG, DEG, and 2,2,2-trichloroethanol were obtained from Restik, United States, while methanol was acquired from Thermo Fisher Scientific, Massachusetts, United States. All chemicals were of analytical grade or the highest available grade. For the validation study, a promethazine syrup was obtained from the local Saudi market. The syrup contained the following ingredients: Promethazine Hydrochloride 5 mg/5 mL (active pharmaceutical ingredient), sodium citrate dihydrate, citric acid monohydrate, disodium ededate, sucrose, orange flavor, essence vanillin, sodium metabisulphate, quinolone yellow, and brilliant blue.

2.1.2. Diluent preparation

A 1.0 μg/mL solution of 2,2,2-trichloroethanol (internal standard) was prepared in methanol. This solution was used as a diluent in the preparation of standards and test solutions.

2.1.3. EG and DEG stock standard solution

A solution containing 20 μg/mL each of EG and DEG was prepared in diluent.

2.1.4. Standard solution

Standard solutions containing 1, 2.5, 5, 7.5, and 10 μg/mL each of EG and DEG were prepared in diluent from EG and DEG standard stock solution.

2.1.5. Test solution from paediatric syrup samples

400 μL of a syrup sample was mixed with 5.0 mL of diluent in a 10.0 mL volumetric flask. The solution was then sonicated and brought up to the mark with the diluent. 3.0 mL of the sample solution was then filtered using a 0.45 μm PTFE filter, and 1 mL of the filtered solution was transferred into a GC vial.

2.2. GC–MS/MS

EG, DEG, and Internal Standard (ISTD) were analyzed using the Shimadzu GC–MS/MS model TQ8050 (Kyoto, Japan), which was equipped with a PAL AOC-000 autosampler. The mass spectrometer operated in the electron impact ionization mode (EI) at 70 eV. The separating column used was Stabilwax-MS (Restek, United States; 0.25 μm, 30 m, and 0.25 mm internal diameter). Data were collected using the LabSolutions software.

2.2.1. GC parameters

The column oven temperature was set to 80 °C and the injection temperature to 250 °C, using splitless injection mode and linear velocity flow control mode. The pressure was set to 65.2 kPa, the total flow was 4.0 mL/min, and the column flow was 1.0 mL/min. Additionally, we used a linear velocity of 36.8 cm/s and a purge flow of 3.0 mL/min. The oven was programmed to have an initial temperature of 80 °C for 1 min, and increased at a rate of 10 °C/min up to 245 °C for 3.5 min.

2.2.2. Mass spectrometry parameters

The ion source temperature was 250 °C, while the interface temperature was 250 °C. The solvent cut time was 6.3 min, and the detector gain was set to 0.1 kV. Both SIM and MRM detection modes were used. For the MRM mode, the following ion transitions were selected: 62.00 > 33.30 m/z (quantifier) and 62.00 > 31.30 m/z (qualifier) for EG; 75.10 > 45.20 m/z (quantifier) and 76.10 > 45.20 m/z (qualifier) for DEG; and 113.00 > 77.00 m/z (quantifier) and 113.00 > 49.00 m/z (qualifier) for ISTD. For the analysis in the SIM mode, the following ions were selected: 31.00, 33.00, and 43.00 for EG; 45.00, 75.00, and 43.00 for DEG; and 31.00, 49.00, and 77.00 for ISTD.

2.3. Method validation

The performance of the method was validated according to the International Council for Harmonisation (ICH) guidelines Q2 (R1) [21]. The following parameters were validated for the analysis of EG and DEG: selectivity, Limit of Detection (LOD), Limit of Quantitation (LOQ), linearity, precision, matrix effect, and accuracy.

2.3.1. Selectivity

To assess the selectivity of the method, unspiked promethazine syrup, the reference standard solutions, and the blank solution were analyzed to evaluate the presence of interfering peaks.

2.3.2. Linearity and range

The linearity of EG and DEG was evaluated by preparing three independent standard calibration curves over the concentration range of 1–10 μg/mL (1, 2.5, 5, 7.5, 10 μg/mL) by diluting the standard stock solution with methanol. The calibration curves were obtained by plotting the peak response ratio of each standard solution relative to ISTD. Linear regression equation ($y = mx + b$) was calculated using the linear least squares regression method. The acceptance criteria for the coefficient of determination was $R^2 > 0.98$. The linear range examined for both EG and DEG was 1–5 μg/mL using spiked promethazine syrup. This range was equivalent to 25–125 μg/mL of EG and DEG in the finished product. This range should cover the potential risks upon human consumption, taking into consideration the permissible daily exposure (PDE) of EG and DEG, the targeted population for each pharmaceutical syrup, and the maximum daily dose.

2.3.3. Limit of Detection (LOD) and Limit of Quantitation (LOQ)

LOD and LOQ corresponded to the concentration levels at which the single-to-noise ratio was >3 and 10, respectively. Signal-to-noise ratios were automatically estimated in the LabSolution software. Six replicates of spiked samples were prepared at the LOQ, and the relative standard deviation (RSD) was calculated. The acceptance criterion was %RSD below 15%.

2.3.4. Accuracy

To evaluate the accuracy, triplicate samples of promethazine syrup spiked with three different concentrations of EG and DEG were prepared (1, 2.5, and 5 μg/mL). The recovery values of the spiked samples (expressed as the percentage of the drug recovered) and the corresponding standard deviations of the triplicate results were calculated for each concentration of EG and DEG. The accuracy acceptance criterion corresponds to 80–120% recovery.

2.3.5. Matrix effect

The matrix effect was determined by comparing the slopes of the calibrations of the standards (solvent-based calibration) and spiked promethazine syrup (matrix-matched calibration) [22,23]. The matrix effect was calculated based on the following formula:

$$\%ME = \frac{Slope_{matrix-matched}}{Slope_{solvent}} \times 100$$

2.3.6. Precision

The repeatability (intra-day precision) was assessed from the spiked recovery experiments by measuring twelve determinations

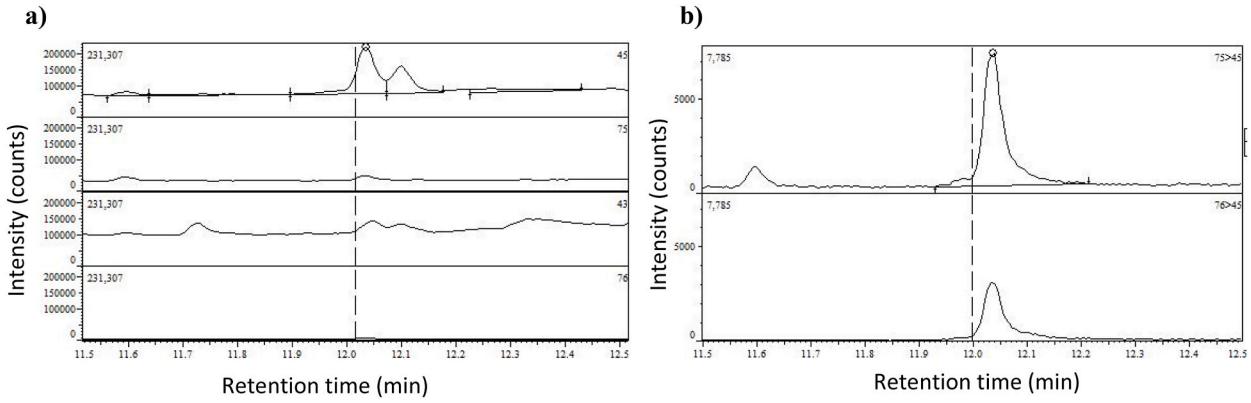

Fig. 1. Comparison between (a) SIM mode and (b) MRM mode in a cough syrup that tested positive for DEG.

Table 1
MRM ion transitions, collision energies and average retention times.

Analyte	Ion transitions	Collision energy (V)	Retention time (minutes)
EG	62.00 > 33.30	2.00	8.201
	62.00 > 31.30	5.00	
DEG	75.10 > 45.20	5.00	12.029
	76.10 > 45.20	7.00	
ISTD	113.00 > 77.00	5.00	9.202
	113.00 > 49.00	10.00	

covering the range of the method (1, 2.5, 5 μg/mL). The method's intermediate (inter-day) precision was assessed by comparing the analytical results of two separate runs of spiked recovery experiments conducted on different days with separate sample preparations. The response ratios of EG and DEG relative to ISTD were calculated, along with their RSDs. The acceptance criteria of the precision are %RSD of no more than 20% and 25% for repeatability and intermediate precision, respectively.

3. Results

3.1. Method development

Several approaches can be employed to enhance the sensitivity of chromatographic methods, such as increasing the concentration of the test analyte or increasing the injection volume. However, this could be problematic since glycerin is a highly viscous liquid. We initially attempted to analyze EG and DEG using the SIM mode. Three ions were selected for each analyte. The selected ions were previously reported by the United States Food and Drug Administration in a published method for analyzing glycols in toothpaste [24]. Although the SIM mode offered high sensitivity, selectivity issues were still present in some samples as the selected ions could be present in different molecules within the matrix (Fig. 1). Furthermore, the same issue existed with EG and ISTD (data not shown). To optimize the selectivity for detecting both EG and DEG, we switched to the MRM mode. The selected ion transitions were chosen based on the paper published by Pérez et al. [25], in which GC–MS/MS was utilized for the analysis of EG, DEG, propylene glycol, and GLY in vaping products.

In the official glycerol USP monograph, 2,2,2-trichloroethanol was utilized as the internal standard and thus was chosen in this study as the ISTD since it was already available in our laboratory and is presumably available in many laboratories. To the best of our knowledge, there have been no previous reports on the analysis of 2,2,2-trichloroethanol using the MRM mode. In this study, several ion transitions were assessed, and the ion transitions that resulted in optimal intensity and selectivity were selected. The MRM mode resulted in slightly lower sensitivity but significantly enhanced selectivity compared to the SIM mode. This decreased the potential interference from the matrix. For our application, the MRM mode was sensitive enough to mitigate potential risks without compromising selectivity.

To improve the intensity of the fragment ions, we evaluated different collision energies. Table 1 summarizes the collision energies that resulted in optimal intensity.

Methanol was chosen as the sole solvent since the samples and the targeted analytes are all soluble in methanol. It has also been used as a diluent in previous studies for glycol analysis in pharmaceutical syrups with no significant limitations to improvement [7]. In the method development phase, we assessed the performance of two columns (Stabilwax-MS and VF-624 ms). The Stabilwax-MS column is more polar compared to the VF-624 ms column, and thus, we hypothesized that it would offer better retention to the targeted analytes. As predicted, EG was almost unretained in the VF-624 ms column, with a retention time of less than 3 min (data not shown). The Stabilwax-MS column offered the best retention away from the solvent cut time, minimizing the risk of detector overload

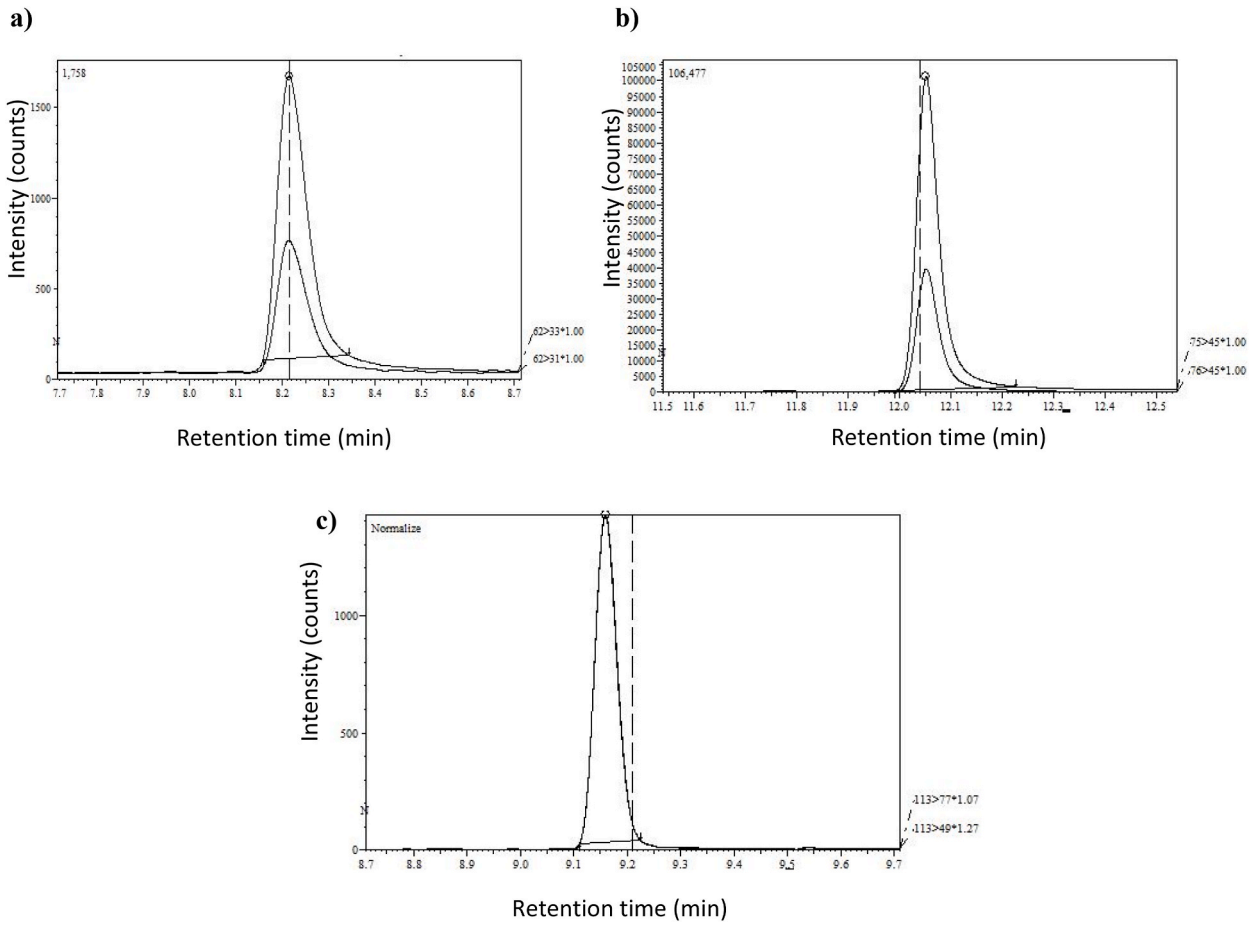

Fig. 2. Promethazine syrup spiked with (a) EG, (b) DEG, and (c) ISTD.

Table 2
Linear regression results for EG and DEG.

Analyte	EG	DEG
Calibration model	Linear regression	
Concentration range	1–10 μg/mL	
Coefficient of determination (R^2)	0.9987	0.9972
Intercept	0.0098	−0.0334
Slope	0.173	7.7761

by the solvent.

3.2. Method validation

3.2.1. Selectivity/specificity

Selectivity was demonstrated by confirming the absence of any interfering peaks in both the unspiked sample of promethazine syrup and the reference standard solutions. Evidently, the peaks of EG, DEG, and ISTD were fully separated (resolution >1.5). Fig. 2 depicts the resolution of the analytes as well as other matrix peaks associated with the promethazine syrup formulation. The analysis proved to be specific and selective for EG and DEG. The method's selectivity was also confirmed for paracetamol, pseudoephedrine, triprolidine, dextromethorphan, and ambroxol drug syrups (data not shown).

3.2.2. Linearity and range

The calibration curves for both EG and DEG standard solutions showed a linear relationship within the selected concentration range of 1–10 μg/mL. The coefficient of determinations for the calibration curves were 0.9981 and 0.9972 for EG and DEG, respectively. The residuals for the calibration curves were randomly distributed across the calibration range, confirming the absence of bias and the

Table 3
Repeatability, intermediate precision, and accuracy results for EG.

EG	Replicates	Run 1 Recovery (%)	Mean Run 1 (%)	Run 2 Recovery (%)	Mean Run 2 (%)
LOQ Spike 1 μg/mL	1	91	93.9	103.8	105.4
	2	88.7		118.6	
	3	88		96.8	
	4	89.4		110.2	
	5	98.3		101.3	
	6	108.3		102.1	
2.5 μg/mL	1	89.7	94.9	113.0	113.9
	2	90.3		116.8	
	3	104.8		111.9	
5 μg/mL	1	85.6	83.9	107.5	101.2
	2	81.3		95.7	
	3	85.0		100.5	
Mean	(n = 12)	91.7		106.5	
%RSD	(n = 12)	8.7		7.1	
Mean	(n = 24)	99.1			
%RSD	(n = 24)	10.8			

Table 4
Repeatability, intermediate precision, and accuracy results for DEG.

DEG	Replicates	Run 1 Recovery (%)	Mean Run 1 (%)	Run 2 Recovery (%)	Mean Run 2 (%)
LOQ Spike 1 μg/mL	1	87.62	84.8	82.22	84.1
	2	85.91		83.97	
	3	83.77		90.88	
	4	83.7		81.8	
	5	85.8		83.3	
	6	82.2		82.7	
2.5 μg/mL	1	91.33	92.36	90.71	92.21
	2	95.77		94.67	
	3	89.98		91.27	
5 μg/mL	1	82.15	86.26	84.78	85.9
	2	88.47		89.03	
	3	88.18		83.9	
Mean	(n = 12)	87		86.6	
%RSD	(n = 12)	4.6		5.1	
Mean	(n = 24)	86.8			
%RSD	(n = 24)	4.7			

linearity of the results. Table 2 summarizes the linear regression results.

3.2.3. Limit of Detection (LOD) and Limit of Quantitation (LOQ)

LOQ for EG and DEG was estimated by the LabSolutions software to be 1 μg/mL, corresponding to a signal-to-noise ratio of >10 and an RSD of less than 15% (Tables 3 and 4). This value is equivalent to 25 μg/mL in the finished product. The LOD for each analyte was 400 ng/mL, which corresponds to a signal-to-noise ratio of >3. This is equivalent to 10 μg/mL in the finished drug product.

3.2.4. Precision

The method's repeatability and intermediate precision were calculated from the spiked recovery experiments. The response ratios of EG and DEG relative to ISTD were calculated, along with their %RSDs. Results are shown in Tables 3 and 4. All %RSD values met the repeatability and intermediate precision acceptance criteria.

3.2.5. Accuracy

The recovery values of the spiked samples and the corresponding standard deviations of the triplicate results for each concentration of EG and DEG are summarized in Tables 3 and 4. The recovery values for each level and the mean calculated from three levels of EG and DEG in each run met the accuracy acceptance criterion of 80–120% recovery.

3.2.6. Matrix effect

%ME was found to be 85% and 113% for DEG and EG, respectively, indicating the presence of matrix-associated ion suppression for DEG and ion enhancement for EG. However, the %ME did not affect the accuracy of the method.

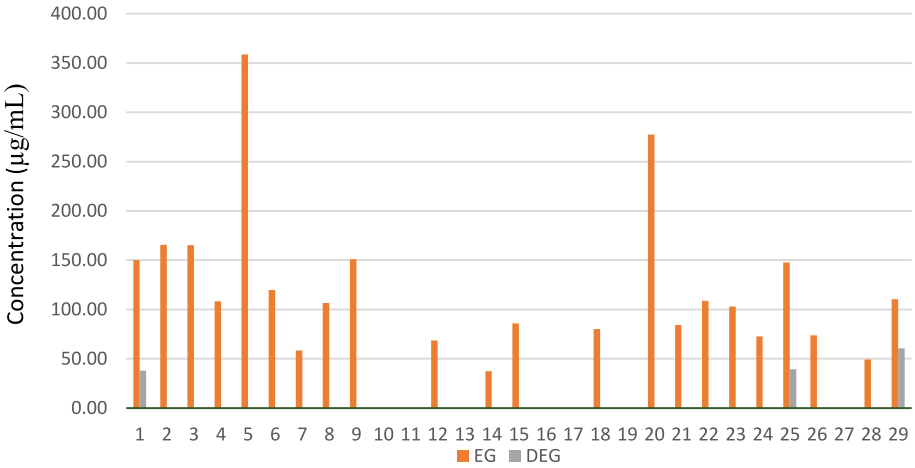

Fig. 3. EG and DEG levels of samples analyzed using MRM mode.

3.3. Application and results interpretation: analysis of drug syrups

The 2022 incident where, in several countries, multiple batches of cough and antihistamine syrups were found to have exceeded the acceptable limits of EG and DEG [11,12,26] led us to proactively assess the safety of the commercially available paediatric syrups distributed in the local market. A total of 29 samples were collected from the local market, representing the majority of cough, antihistaminic, and antipyretic syrups distributed in the Saudi market. The active pharmaceutical ingredients of these samples were promethazine, paracetamol, pseudoephedrine, triprolidine, dextromethorphan, and ambroxol drug syrups. The samples originated from several countries, namely Saudi Arabia, Kuwait, Jordan, India, and France. Samples were analyzed in duplicate using the SIM and MRM modes.

Out of the 29 drugs that were tested, 22 were above the quantitation limit for EG, and only three were above the quantitation limit for DEG. The drugs that tested positive for DEG were also found to be positive for EG. The results are shown in Fig. 3. Both the European Pharmacopoeia and USP have specified limits for EG and DEG. The USP limit for EG and DEG in GLY raw material is not more than 0.1% [13] and no more than 0.25% in PEG raw material for the combined amount of EG and DEG [14]. The European Pharmacopoeia limit for DEG in GLY is 0.1%, and for PEG, it is 0.4% for EG and DEG combined [15]. EG is classified as a class 2 solvent, according to the ICH. This class comprises solvents that need to be restricted in pharmaceutical products because of their inherent toxicity. The PDE for EG is 6.2 mg/day. It is noteworthy that this threshold was estimated for an adult weighing 50 kg, and it was crucial to adjust it for paediatric weight in this investigation. There is no stated limit for DEG in the ICH [27]. A risk-based approach was applied to determine the risk of exposure to these syrups, taking into consideration the PDE, the targeted population of each medication and the maximum daily dose, and none of the tested samples exceeded the limits for EG and DEG.

4. Discussion

The recurring incidents of glycol mass poisonings necessitated the development of a method capable of analyzing EG and DEG in a wide range of pharmaceutical syrups in a timely manner. The official USP method for EG and DEG analysis in GLY and PEG utilizes GC-FID and is intended for raw materials analysis. This could be challenging when attempting to analyze finished products with more complex matrices as interferences from the matrix might occur. GC–MS/MS analysis in the MRM mode was virtually selective in all the samples that we analyzed compared to the SIM mode. The absence of matrix interference in the MRM mode enabled the performance of routine automatic integration. Nevertheless, it should be noted that the selected quantifier and qualifier ion fragments for EG and DEG in this study were relatively less abundant ion fragments and thus might present a challenge when attempting to quantify EG and DEG in samples with low concentrations of these analytes. Increasing the injection volume or increasing the concentration of the sample might solve this issue. However, due to the viscous nature of the samples, increasing the sample's concentration could be problematic in some cases.

As mentioned previously, EG and DEG could be present in any GLY, PEG, or sorbitol-based pharmaceuticals, including cough, antihistaminic, and antipyretic syrups. Historically, glycol mass poisonings were more frequently associated with these drug classes, and hence, attention to these medications were given in this study. However, the safety of other pharmaceutical syrups will also be assessed in the future. It should also be noted that the presence of DEG in the abovementioned pharmaceuticals could be due to the intentional substitution of GLY with DEG or as a by-product during the manufacturing process of GLY and other high-risk diluents [28].

Most recent glycol mass poisoning occurred in developing countries with limited resources and unavailability of advanced analytical instruments. As mentioned previously, several methods were reported for glycol analysis in pharmaceuticals. Some are more suitable for the initial screening of pharmaceutical syrups suspected to be contaminated with glycols and could provide valuable insights where resources are limited. These methods are summarized in Table 5.

Table 5
A general comparison between the developed GC–MS/MS method and previously reported methods for glycols analysis in pharmaceuticals.

Analytical method	Analyte	Matrix	Sample preparation
The developed GC–MS/MS method	EG, DEG	Antipyretics, antihistaminic, and cough syrups.	Samples were diluted in methanol.
HPLC-MS/MS [7]	DEG	Paracetamol, antihistamines, expectorants, antacids, and vitamin preparations	Paracetamol samples were diluted in methanol, whereas the rest of the samples were diluted in methanol/water (1:10).
FT-IR and NIR [17]	DEG	Glycerin-based cough Syrups	Samples were analyzed after spiking them with DEG (without dilution or derivatization)
HPLC-UV [29]	DEG, propylene glycol (PG)	Paracetamol and cough syrups	A pre-column derivatization step with TSIC was conducted to enable UV detection.
GC-FID [13]	EG, DEG	GLY raw material	GLY was diluted in methanol
GC-FID [14]	EG, DEG	PEG raw material	PEG was diluted in water

In general, most methods reported simple sample preparation procedures in which syrups were extracted in one solvent, with no derivatization needed, except for one study that reported the utilization of *p*-toluenesulfonyl isocyanate (TSIC) as a derivatization reagent before HPLC analysis to enable UV detection of DEG and propylene glycol in pharmaceutical products [29]. Some methods were developed to detect DEG only. Therefore, laboratories might want to consider further developing the method to detect EG before transferring the method into their laboratory, since EG was also implicated in recent glycols poisonings. Besides pharmaceuticals, several methods are reported for glycol analysis in different matrices, such as human plasma, vaping products, and antifreeze agents analysis in runoff water, food, and cosmetics samples [18,24,25,30,31]. We believe that the developed GC–MS/MS method could be applicable to other applications other than pharmaceuticals. However, the method should be validated to fit the intended purpose.

5. Conclusion

In this study, we reported a new method using GC–MS/MS for the determination and quantification of EG and DEG in paediatric syrups. This method provided many advantages, such as improved selectivity, efficient separation between EG and DEG, and the lack of glycol derivatization or sample cleanup. Full method validation was conducted utilizing negative samples of promethazine syrup. The method proved to be selective for paediatric syrups that contain the following active pharmaceutical ingredients: paracetamol, pseudoephedrine, triprolidine, dextromethorphan, and ambroxol. The method reported in this study is recommended for laboratories conducting analyses on samples suspected to be contaminated with glycols.

Disclaimer

The views expressed in this paper are those of the author(s) and do not necessarily reflect those of the SFDA or its stakeholders. Guaranteeing the accuracy and validity of the data is the sole responsibility of the research team.

Data availability statement

Data will be made available on request.

CRediT authorship contribution statement

Monerah A. Altamimy: Writing – original draft, Validation, Methodology, Investigation, Formal analysis. **Yahya M. Alshehri:** Writing – review & editing, Supervision, Project administration, Methodology, Conceptualization. **Fahad S. Aldawsari:** Writing – review & editing. **Norah H. Altalyan:** Writing – original draft, Investigation. **Sultan K. AlShmmari:** Investigation. **Shaikah F. Alzaid:** Investigation. **Naif A. Al-Qahtani:** Conceptualization. **Turki M. Alsagoor:** Conceptualization. **Mobarak S. Al Shahrani:** Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We would like to thank the staff at the National Drug and Cosmetic Control Laboratory (NDCCL) of SFDA for their support in coordinating the work on the analytical instruments as well as granting access to other laboratory equipment.

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