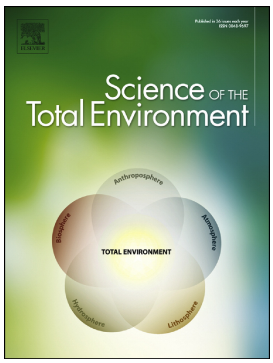

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Myriam Borgatta, Julie Hechon, Pascal Wild, Nancy B. Hopf

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Influence of collection and storage materials on glycol ether concentrations in urine and blood

Myriam Borgatta[1,*], Julie Hechon[2], Pascal Wild[1,3], and Nancy B Hopf[1]

[1]Center for Primary Care and Public Health (Unisanté; formerly known as Institute for Work and Health - IST), University of Lausanne, Switzerland; Nancy.Hopf@unisante.ch; Myriam.Borgatta@unisante.ch

[2]@work performed while employed at IST. Julie.Hechon@gmail.com

[3]Institute for Research and Safety (INRS), Vandoeuvre les Nancy, France; pascal.wild@inrs.fr

*****Correspondence: Myriam.Borgatta@unisante.ch; +41 (0) 21 314 9558

Abstract: Glycol ethers, such as propylene glycol monomethyl ether (PGME) and propylene glycol monobuthyl ether (PGBE) are solvents found in many professional and domestic products. In biomonitoring studies, the type of materials used to collect, store, and transport these samples can greatly influence the analytical results because materials can adsorb the analyte. Plastic tubes generally have a hydrophobic internal surface that can reduce the concentration of certain chemicals and result in an underestimation of workers' exposures. The aim of this study was to assess whether the storage of PGME and PGBE spiked blood and urine samples led to different PGME and PGBE concentrations in vials made of glass and common plastics (polypropylene (PP), polyethylene (PE) or polystyrene (PS)). Glycol ether concentrations were quantified with headspace gas chromatography equipped with a flame ionization detector. Our results show stable urinary PGME and PGBE concentrations in PP, while up to 15% variations in urinary PGME for PE and PS. For PGME and PGBE in blood, we observed no statistically significant losses in glass, while losses were recorded for all types of plastic tested (PS, PP and PE). We conclude that biomonitoring samples should be collected in glass for blood and PP for urine.

Keywords: biomonitoring, measured concentration, urinary level, blood sample, occupational exposure, analytical analysis

1. Introduction

The materials used to collect, store and transport body fluids, such as blood and urine, can adsorb the analyte with great influence on the analytical results and consequently, resulting decisions (Bowen et al., 2010; Bowen and Remaley, 2014). Plastic tubes generally have a hydrophobic internal surface that may reduce the concentration of certain chemicals of interest in analyzed fluids (Bowen and Remaley, 2014). This adsorption phenomenon is explained by the binding of a certain amount of a chemical to the inner wall of containers (Fukazawa et al., 2010). This surface can interact with a limited amount of a chemical (Palmgrén et al., 2006). The lower the concentration of the free chemical the greater is the observable loss. Validation studies should include sample vial materials, as these are crucial in generating reliable results. Vial material should not contribute to analytic interferences, but should fit the purpose and satisfy the particular requirements for its specific intended use. Uncertainties in the analyte amount in a sample can lead to disastrous results as crucial safety decisions are made based on these. In medicine, blood and urine are collected to measure the level of a pharmaceutical in patients to adjust the therapeutic dose (Bowen et al., 2016). In toxicological studies, a chemical can also be quantified in blood and urine to determine a dose-effect relationship (Hopf et al., 2012), which helps authorities to set chemical health based exposure limit values (Federal Office of Public Health (FOPH), n.d.). For example, occupational biological limit values exist to protect workers' health (Chen and Lippmann, 2015; European Chemicals Agency (ECHA), n.d.), and the actions needed to reduce exposures are made on the magnitude of the parent chemical or its metabolite in worker's blood and urine. Human

biomonitoring programs in the general population are also conducted across continents to understand the average body burden of some chemicals of interest. Up to 75% of the analytical magnitude of error are during a pre-analytical phase (Bowen et al., 2016), which includes biological fluid collections, storage and transport of samples, and the type of biological media and analyte that will be analyzed. Among these variables that can introduce errors in the pre-analytical phase, material is often under-recognized or neglected (Bowen et al., 2010; Bowen and Remaley, 2014). Nowadays, plastic collecting and storage containers often replace glass for occupational safety as well as sample safety reasons (Bowen et al., 2016, 2010; Ernst, 2001). Materials used to collect and store blood and urine are mainly made of three common polymer plastics, such as polypropylene (PP), polyethylene (PE) or polystyrene (PS) (Boeynaems et al., 2004; Bowen et al., 2005; Bowen and Remaley, 2014; Kratz et al., 2006). For instance, in biomonitoring and toxicological studies with glycol ethers, the material used was either polyethylene (Corley et al., 1997; Devanthéry et al., 2000; Moffatt et al., 1986) or glass (Domoradzki et al., 2003), or was even not reported (Angerer et al., 2002; Devanthéry et al., 2002; Hubner et al., 1992; Johanson et al., 1986; Juenke et al., 2011; Livesey et al., 1995; Morgott and Nolan, 1987; Robertson and Loosli, 1947; Smallwood et al., 1984; Starek et al., 2010; Suber et al., 1989). Glycol ethers is a family of 80 chemicals that may be reprotoxic and neurotoxic (Fowles et al., 2017; Institut national de la santé et de la recherche médicale, 2005; Institut National de Recherche et de Sécurité, 2012; Landry et al., 1983; Lemazurier et al., 2003; US EPA, n.d.; Welsch, 2005). Glycol ethers are used as amphiphilic solvents in manufacture of paints and in the formulation of a wide range of products, such as glues, inks, varnishes, cosmetics, cleaning and metallurgical products (e.g., degreasers, cutting fluids) (Agency for Toxic Substances and Disease Registry, n.d.; Institut national de la santé et de la recherche médicale, 2005). Handling these may result in exposures (Ben-Brik et al., 2004; Devanthéry et al., 2000; Johanson, 1988; Welch et al., 1988). The potential for inhalation and skin uptake make biomonitoring an excellent tool to quantify total internal dose capturing both routes of entry. Dose estimates are an important part of risk assessment (Albertini Richard et al., 2006; Sexton et al., 2004). Propylene glycol monomethyl ether (PGME, CAS no. 107-98-2) and propylene glycol monobuthyl ether (PGBE, CAS no 5131-66-8) are two glycol ethers found in abundant domestic and professional products (Agence française de sécurité sanitaire de l'environnement et du travail (afsset), 2008; Institut national de l'environnement industriel et des risques (INERIS), 2007). As with other glycol ethers, there is no guideline that indicates the type of materials to be used to sample blood and urine. Inappropriate materials may therefore lead to erroneous results such an underestimation of PGME and PGBE concentrations in the analyzed samples.

Both PGME and PGBE are biomarkers of exposure and can be quantified directly as such in blood and urine. The aim of this study was to assess whether the storage of blood and urine samples between 6 hours and 7 days in the common plastics PP, PS, and PE, and in borosilicate glass (G) tubes led to different PGME and PGBE concentrations.

2. Materials and Methods

Chemicals: PGME (≥ 99%), PGBE (≥ 99%) and propylene glycol propyl ether (PGPE, CAS 1569-01-3, 99%) were obtained from Sigma Aldrich (Buchs SG, Switzerland), sodium sulphate Na_2SO_4 (CAS 7757-82-6) from Merck (Darmstadt, Germany).

Biological samples: PGME and PGBE concentrations in blood and urine were measured in four common collecting and storage materials for body fluids: borosilicate glass (G), polypropylene (PP), polystyrene (PS) and polyethylene (PE). The vials were 5 mL, 75 mm high and 12 mm diameter. G vials were obtained from Labmaterials (www.labmaterials.net, article N°: STUN-001-250), PP and PS vials from Sarstedt (www.sarstedt.com, article N° 55.526 and N° 55.476 for PP and PS, respectively), and PE vials from Huberlab (www.huberlab.ch, article N°7.115 301).

Experimental design: The experimental design is summarized in Figure 1. Anticoagulated blood was used in this study. Blood and urine were spiked (stock solutions) with PGME or PGBE at two concentrations: A and B. These concentrations were obtained in a human controlled study where participants (n=11) were exposed 6 hours to 129 mg/m^3 (35 ppm) and 81 mg/m^3 (15 ppm) of PGME and PGBE, respectively (data not shown, ongoing study). Blood and urine samples were collected during and after participants' exposure. The concentration A corresponded to low concentrations observed in blood and urine (around 0.4 mg/L), whereas

concentration B represents high PGME concentrations quantified in urine (around 4 mg/L). The stock solution was first prepared in a 200 mL glass beaker, and then directly into headspace (HS) glass vials to provide controls (t0, in three replicates). The rest of the stock solution (2 mL of blood or 2.2 mL of urine) was transferred into G, PP, PS and PE vials in four replicates for each storage time. Blood and urine was never in contact with the cap. The pipette tip was changed at each pipetting. PGME and PGBE quantification was performed after 6h (t1), 24h (t2) and 168h (t3 one week) of storage in the refrigerator (4°C). These times represent the storage laps times frequently observed before laboratory analysis during toxicological studies.

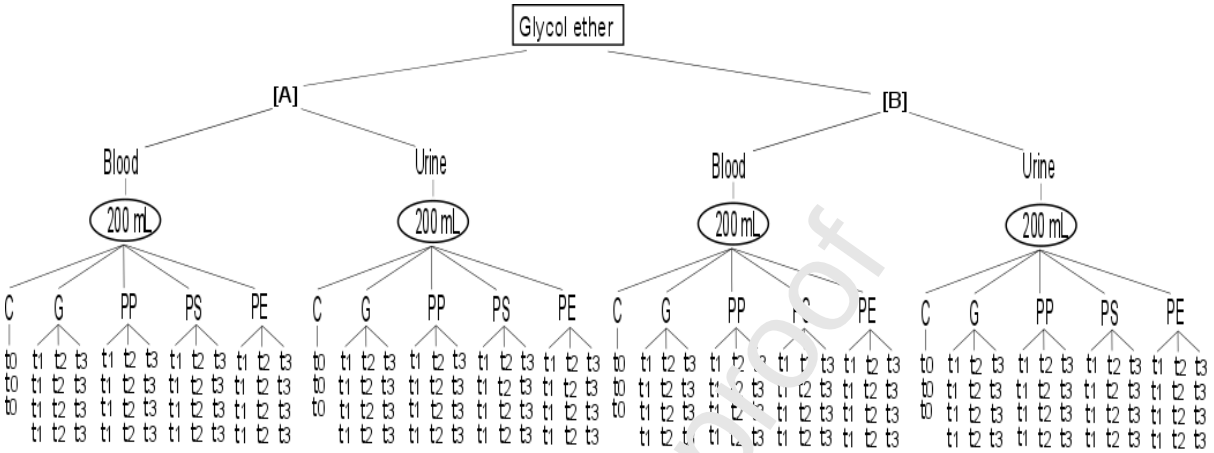

Figure 1: Experimental design with four common materials used to collect and store blood and urine: Glass (G), polypropylene (PP), polystyrene (PS), and polyethylene (PE). Blood and urine were spiked with PGME or PGBE in a 200 mL glass beaker. PGME and PGBE quantification in blood and urine was performed before any contact with the tested material (t0 and control (C)) and after 6h (t1), 24h (t2) and 168h (t3) of contact (n=204).

Calibration curve solutions: PGME and PGBE stock solutions for calibration curves were prepared with deionized water (Milli-Q® Advantage A10) at the concentration of 2 g/L. The stock solutions were prepared in glass flasks and stored in the refrigerator (4°C). PGME and PGBE stock solutions were later diluted in blood or urine to run a series of minimum six calibration points across a range of concentrations from 0.1 mg/L to 5 mg/L. Limit of quantification (LOQ) was 0.04 mg/L.

Internal standard solutions: The internal standard (IS) was PGPE in water (2 g/L). The IS was diluted 20-times and was added (50µL) to the analytical vials containing blood (2 mL), urine (2.2 mL), water (blank) (2 mL), and calibration solution (2 mL). The IS was deliberately added at the end to avoid a possible adsorption to the material.

Glycol ether analysis: An analytical method combining automated headspace (HS) solid-phase microextraction (SPME) sampling techniques was optimized (Tomicic and Berode, 2010). At t1, t2 and t3, 1 mL of blood was transferred into 20-mL injection Headspace (HS) glass containing 1 mL of MilliQ water and IS. For urine, 1gr of Na_2SO_4 was weighted in 20-mL injection HS and 2 mL of urine plus IS were added. No Na_2SO_4 were needed for blood. Blood samples were diluted in water (1:1) to reduce coagulation effect and increase the sensitivity. PGME and PGBE in blood and urine were analyzed and quantified with gas chromatography (GC) (Agilent Technologies AG, Urdorf, Switzerland) equipped with MultiPurposeSampler MPS2 (Gerstel AG, Sursee, Switzerland) and flame ionization detector (280 °C). HS glass vials containing urine or blood samples were incubated 10 min at 55°C or 90°C, respectively. Extraction was performed for 2 min using a solid phase microextraction (SPME, fiber carboxen/polydimethylsiloxane, CAR/PDMS, 75µm, Supelco, Buchs, Switzerland). The fiber was desorbed (250°C) and transfered onto the column (Optima® FFAP plus, 15 m; 0.5 µm film thickness, 0.32 mm ID; Macherey Nagel, Oensingen, Switzerland) in splitless mode at a flow rate of 1.5 ml/min. The GC temperature program was to 40°C (1 min), raised (11.43°C/minute) to 120°C, and held for 1 min (total cycle time of 8.99 min). Under these conditions, retention time was 5.19 min for PGME and 7.56 min for PGBE. Limit of quantification (LOQ) was 0.04 mg/L.

Statistical analysis: There is a mean +/- 15% analytical uncertainty with the HS SPME technique. This is the variability we accept in this paper and is according to the U.S. food and drug administration (FDA)'s guidance (Food and Administration (FDA), 2001). The variability of the respective concentration of PGME and PGBE in

blood and in urine was analysed using a standard anova with the time point and the storage material and their interaction as independent factors. The concentration was expressed in percentage of the mean concentration at t0 so that the target concentration was 100%. Statistical analyses were performed using Stata software (StataCorp LP, College Station, TX, USA).

3. Results

The concentrations (raw data) of PGME and PGBE in blood and urine are summarized in Table 1 and Table 2.

Table 1: Blood concentrations of PGME and PGBE after 6-h, 24-h and 168-h of storage in PE, PS, PP and glass vials. Control was performed before any contact with the tested tube material. The concentrations are in mg/L.

	Molecule	Tube material	Control 0h (n=3)		6h (n=4)		24h (n=4)		168h (n=4)	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD
Concentration A	PGME	PE	0.413	0.014	0.354	0.013	0.354	0.003	0.311	0.004
		PP			0.356	0.013	0.347	0.015	0.318	0.013
		PS			0.345	0.020	0.359	0.021	0.339	0.006
		Glass			0.358	0.010	0.376	0.014	0.376	0.015
	PGBE	PE	0.485	0.018	0.427	0.009	0.437	0.029	0.369	0.040
		PP			0.449	0.013	0.474	0.009	0.480	0.012
		PS			0.452	0.009	0.471	0.011	0.490	0.016
		Glass			0.436	0.019	0.461	0.018	0.464	0.011
Concentration B	PGME	PE	4.847	0.045	4.889	0.132	4.831	0.033	4.599	0.102
		PP			4.920	0.059	4.871	0.075	4.639	0.142
		PS			4.785	0.172	4.924	0.041	4.728	0.134
		Glass			4.609	0.172	4.779	0.080	4.773	0.208
	PGBE	PE	5.014	0.073	4.992	0.152	4.807	0.445	4.653	0.324
		PP			4.739	0.181	4.723	0.215	5.127	0.077
		PS			4.910	0.075	5.043	0.242	5.348	0.129
		Glass			4.894	0.154	5.009	0.254	4.940	0.345

Table 2: Urine concentrations of PGME and PGBE after 6-h, 24-h and 168-h of storage in PE, PS, PP and glass vials. Control was performed before any contact with the tested tube material. The concentrations are in mg/L.

	Molecule	Tube material	Control 0h (n=3)		6h (n=4)		24h (n=4)		168h (n=4)	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD
Concentration A	PGME	PE	0.397	0.021	0.391	0.014	0.372	0.024	0.423	0.051
		PP			0.403	0.007	0.401	0.011	0.354	0.060
		PS			0.410	0.025	0.412	0.018	0.464	0.084
		Glass			0.415	0.011	0.397	0.028	0.290	0.038
	PGBE	PE	0.347	0.009	0.344	0.006	0.344	0.006	0.358	0.002
		PP			0.347	0.009	0.348	0.015	0.356	0.012
		PS			0.335	0.007	0.347	0.012	0.345	0.007
		Glass			0.338	0.004	0.349	0.007	0.332	0.015
Concentration B	PGME	PE	5.184	0.087	5.718	0.338	6.061	0.139	5.784	0.341
		PP			5.666	0.256	5.844	0.425	5.429	0.293
		PS			5.942	0.264	6.146	0.175	5.587	0.878
		Glass			5.467	0.131	5.444	0.312	4.979	0.200
	PGBE	PE	3.572	0.058	3.705	0.119	3.829	0.104	3.601	0.097
		PP			3.626	0.040	3.657	0.147	3.630	0.089
		PS			3.517	0.124	3.727	0.174	3.571	0.165
		Glass			3.495	0.152	3.602	0.085	3.636	0.058

Figure 2 and Figure 3 summarize the variability (%) of PGME and PGBE concentrations according to materials and storage time. In blood, no statistically significant difference between materials for PGME and PGBE was observed when this biological fluid was stored in glass (concentration A ($p < 0.14$), concentration B ($p < 0.29$)). The plastic PS lost 16.5 % of PGME at blood concentration A after 6-h, and 18% after a week. In PP and PE, PGME blood concentration A decreased with time and after a week of storage, and the losses were 25% and 23%, respectively. At the same concentration, PE showed also a loss of 24% of PGBE in blood after a week at this concentration.

The results in urine showed no statistically significant difference between materials for PGME and PGBE when the body fluid was stored in PP. At the PGME concentration B in urine, differences of 17% and 19% were observed for PE and PS after 24h. At the lowest test concentration (i.e, concentration A), one week of storage in PS increased PGME concentrations in urine by 17% and decrease it by 27% in glass.

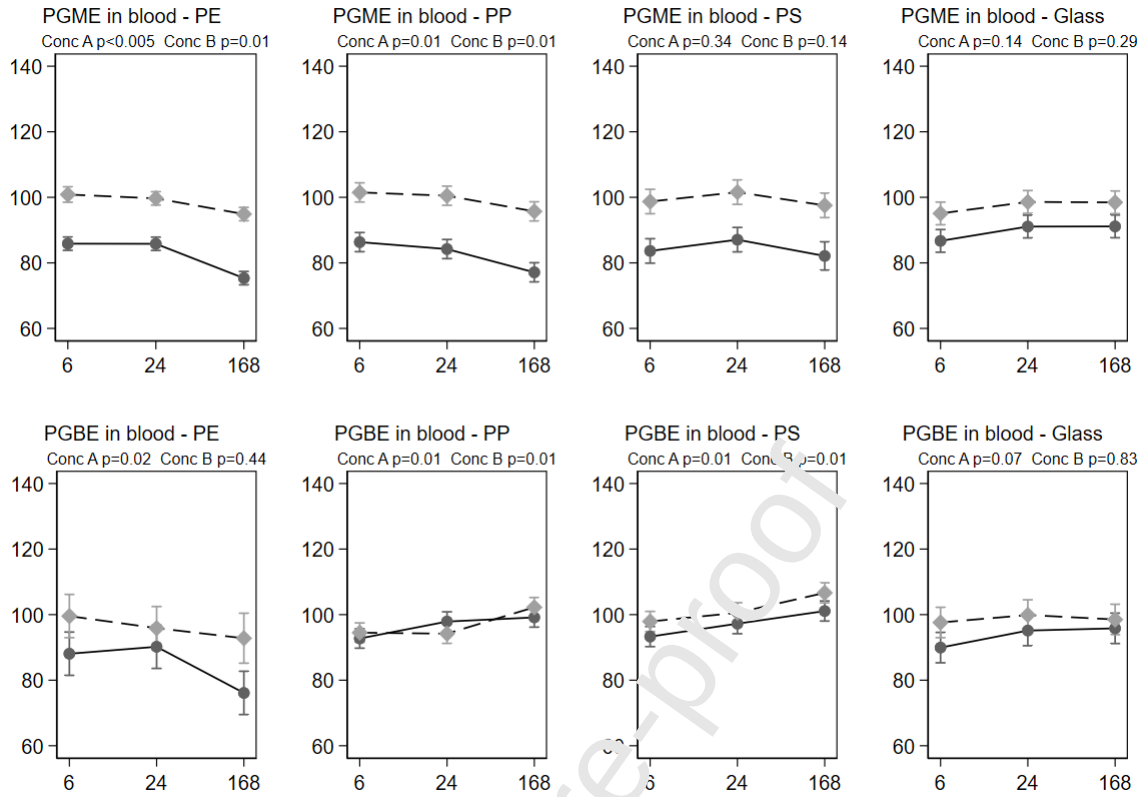

Figure 2: PGME and PGBE concentrations expressed in per cent of the initial concentration (mean and 95% CI) in blood (y-axis) in PE, PS, PP and glass vials after 6-h, 24-h and 168-h of storage (x-axis). The solid line is the lowest concentration A and the dashed line is the highest concentration B. Statistical significances (p values for one-way anova test of differences between storage times) are indicated below the individual graphs.

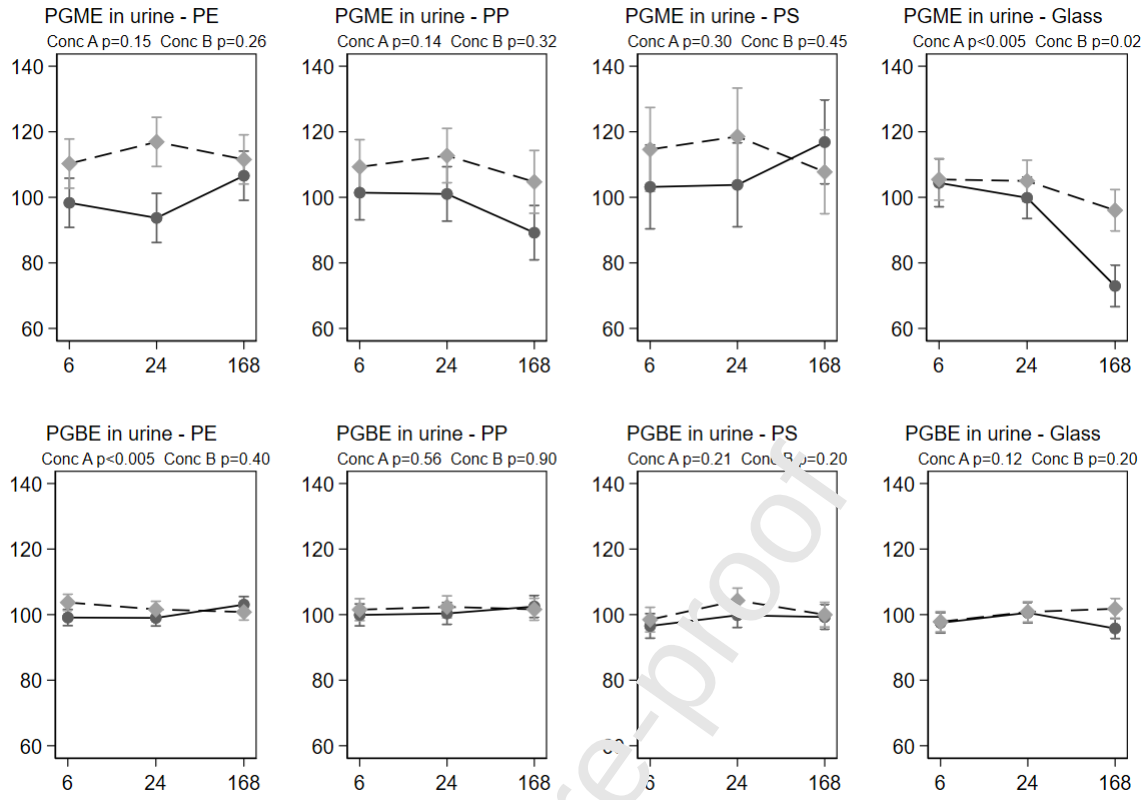

Figure 3: PGME and PGBE concentrations expressed in percent of the initial concentration (mean and 95% CI) in urine (y-axis) in PE, PS, PP and glass vials after 6-h, 24-h and 168-h of storage (x-axis). The solid line is the lowest concentration A and the dashed line is the highest concentration B. Statistical significances (p values for one-way anova test of differences between storage times) are indicated below the individual graphs.

4. Discussion

Our results showed that glass was the best material to store blood as and PP for urine samples when analyzing PGME and PGBE. Biomonitoring and toxicological studies require reliable analytical results to verify the chemical exposure and should thus consider sampling material in their protocols. The greatest differences in PGME and PGBE concentrations were observed for blood contained in PE. This plastic material is known to also perform poorly for chlorinated hydrocarbons, aromatic compounds and strong acids (National Institute for Occupational Safety and Health (NIOSH), 2021). Consequently, we recommend not using this material for either urine or blood samples.

Significant concentration differences exist for PGBE in blood but not in urine suggesting a biological matrix effect at least for this substance. The small variations (i.e., ≤ 15%) observed around the control (expressed as 100%) such as the increases in PGME and PGBE concentrations in some samples likely indicate an intrinsic variability due to the chemical analysis. Evaporation or degradation of PGME and PGBE was unlikely to occur in our study. PGME and PGBE are miscible in water (amphiphilic) and relatively non-volatile from water. PGME is known to have a biodegradation longer than 28 days in water (US EPA, n.d.) and since PGBE has similar chemical properties to PGME, we reasonably assume the same for this molecule. The losses measured in the lowest (i.e., concentration A) were more pronounced than in the highest (i.e,. concentration B) concentration, which is in line with Palmgrén et al., 2006 for other chemicals. In blood, no loss of PGME and PGBE was observed in glass tubes, indicating that this material did not interact with these chemicals. Glass was therefore deemed the best material for blood collection and storage. In forensic toxicology for example, blood samples are regularly collected into glass tubes to minimize drug adsorption (Kerrigan, 2013). Vials made in

glass are also known to minimize volatile analyte loss such as solvents (Steven B. Karch, 2007). Glass was also a good material for urine storage when PGME and PGBE were present at the highest test concentration (i.e, concentration B). However, a substantial decrease of PGME concentration in urine was observed after a week of storage in glass for the lowest test concentration (i.e, concentration A). This loss occurred at a concentration 10-fold higher than the LOQ and the results were therefore considered as reliable, especially within the narrow concentration range that was tested in this study (between concentration A and B, see Table 1). PP was a better material than glass to store the urine as no losses were observed, whatever the concentration and time of storage. Plastic materials are often preferred in biomonitoring since it decreases the risk of the glass breaking as well as a decreased weight. In general, a decrease in the concentration of a chemical is expected in plastic materials, not in glass, and is attributed to adsorption phenomenon (Beitz et al., 1999). In our study, the use of glass was appropriate for blood but not for urine. The PP plastic was a better material than glass to store urine and this result emphasizes the importance of assessing the sampling materials and selecting the appropriate material prior biomonitoring and toxicological studies.

The material used to collect and store biological samples are often not reported in toxicological and biomonitoring studies (Angerer et al., 2002; Devanthéry et al., 2002; Hubner et al., 1992; Johanson et al., 1986; Juenke et al., 2011; Livesey et al., 1995; Morgott and Nolan, 1987; Robertson and Loosli, 1947; Smallwood et al., 1984; Starek et al., 2010; Suber et al., 1989). For example, in a biomonitoring study with workers, Hubner et al., 1992 collected blood and urine to assess occupational exposures to PGME in a brakehose production plant. Workers were exposed to 22.3 ppm of PGME, and the internal PGME dose was 13.5 mg/L in blood and 4.6 mg/L in urine (storage time was not mentioned). Assuming the samples were collected in common plastic tubes such as PE, and using our results, then the Hubner et al. study results would have underestimated the internal exposure of the workers from 10-25% depending on the amount. Conversely, the use of PS for urine would have overestimated the concentration of about 19% at 24h storage. Both, an underestimation and overestimation of the exposure can lead to inappropriate decisions for the protection of workers' health.

Our study faced certain limitations, particularly at the experimental design level. The biological fluids were spiked once in a large glass beaker and distributed into the test material tubes. As all the samples were ready to be analyzed at the same time this introduced a waiting time in the GC. These differences in injection time could potentially have introduced concentration errors. Another option would have been to spike the biological fluid in a time-delayed manner. However, this procedure could possibly introduce a pipetting variability and interfere with the objective of the study, which was to determine potential concentration errors due to biological fluid storage over time. In a preliminary test, we confirmed that the glycol ether concentrations did not change when kept in glass vial in the GC auto sampler at room temperature for 24 hours (data not shown). This study could be used as a protocol to test for possible concentration errors in biological fluids.

5. Conclusions

We conclude that the best collection materials to quantify PGME and PGBE in biological samples were glass for blood and PP for urine. Storage duration at 4°C will have an impact on PGME and PGBE concentrations in urine. Laboratories that cannot process the samples immediately or at least within 24 hours after reception should quantified possible losses of glycol ethers in frozen samples. We recommend using these collection materials with other propylene glycol ethers in biological fluids as they have similar chemical properties as PGME and PGBE..

Author Contributions:

Author	**CRediT**
Borgatta Myriam	Conceptualization, Methodology, Writing- Original draft preparation, Visualization, Project administration, Funding acquisition.

Wild Pascal	Formal analysis, Visualization, Review & Editing
Hechon Julie	Methodology, laboratory analyses
Nancy Hopf	Methodology, Visualization, Funding acquisition, Writing - Review & Editing, Supervision

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References

Agence française de sécurité sanitaire de l'environnement et du travail (afsset), 2008. Les éthers de glycol - Synthèse des connaissances sur les expositions de la population générale et professionnelle en France (No. 2003/016). Maisons-Alfort, France.

Agency for Toxic Substances and Disease Registry, n.d. Public Health Statement: Propylene Glycol [WWW Document]. URL www.atsdr.cdc.gov/phs/phs.asp?id=1120&tid=240 (accessed 3.16.16).

Albertini Richard, Bird Michael, Doerrer Nancy, Needham Larry, Robison Steven, Sheldon Linda, Zenick Harold, 2006. The Use of Biomonitoring Data in Exposure and Human Health Risk Assessments. Environ. Health Perspect. 114, 1755–1762. https://doi.org/10.1289/ehp.9056

Angerer, J., Göen, T., Hubner, B., Weiß, T., 2002. Propylene and diethylene glycol ethers [Biomonitoring Methods, 2007], in: The MAK-Collection for Occupational Health and Safety. Wiley-VCH Verlag GmbH & Co. KGaA.

Beitz, C., Bertsch, T., Hannak, D., Schrammel, W., Einberger, C., Wehling, M., 1999. Compatibility of plastics with cytotoxic drug solutions-comparison of polyethylene with other container materials. Int. J. Pharm. 185, 113–121. https://doi.org/10.1016/s0378-5173(99)00175-1

Ben-Brik, E., Jérôme, L., Arnaud, I., Yous, S., Labat, L., Haguenoer, J.M., Multigner, L., 2004. Exposure to glycol ethers in a population of French men evaluated by measurement of urinary alkoxycarboxylic acids. Int. Arch. Occup. Environ. Health 77, 368–372. https://doi.org/10.1007/s00420-004-0523-4

Boeynaems, J.-M., De Leener, A., Dessars, B., Villa-Lobos, H.R., Aubry, J.-C., Cotton, F., Thiry, P., 2004. Evaluation of a new generation of plastic evacuated blood-collection tubes in clinical chemistry, therapeutic drug monitoring, hormone and trace metal analysis. Clin. Chem. Lab. Med. 42, 67–71. https://doi.org/10.1515/CCLM.2004.013

Bowen, R.A.R., Chan, Y., Cohen, J., Rehak, N.N., Hortin, G.L., Csako, G., Remaley, A.T., 2005. Effect of blood collection tubes on total triiodothyronine and other laboratory assays. Clin. Chem. 51, 424–433. https://doi.org/10.1373/clinchem.2004.043349

Bowen, R.A.R., Hortin, G.L., Csako, G., Otañez, O.H., Remaley, A.T., 2010. Impact of blood collection devices on clinical chemistry assays. Clin. Biochem. 43, 4–25. https://doi.org/10.1016/j.clinbiochem.2009.10.001

Bowen, R.A.R., Kim, S.C., Settayapiwat, A., Austria-Esguerra, V., Zare, R.N., 2016. Performance of chemically modified plastic blood collection tubes. Clin. Biochem. 49, 90–99. https://doi.org/10.1016/j.clinbiochem.2015.09.003

Bowen, R.A.R., Remaley, A.T., 2014. Interferences from blood collection tube components on clinical chemistry assays. Biochem. Medica 24, 31–44. https://doi.org/10.11613/BM.2014.006

Chen, L.-C., Lippmann, M., 2015. Inhalation Toxicology Methods: The Generation and Characterization of Exposure Atmospheres and Inhalational Exposures. Curr. Protoc. Toxicol. 63, 24.4.1-24.4.23. https://doi.org/10.1002/0471140856.tx2404s63

Corley, R.A., Markham, D.A., Banks, C., Delorme, P., Masterman, A., Houle, J.M., 1997. Physiologically Based Pharmacokinetics and the Dermal Absorption of 2-Butoxyethanol Vapor by Humans. Toxicol. Sci. 39, 120–130. https://doi.org/10.1093/toxsci/39.2.120

Devanthéry, A., Berode, M., Droz, P.-O., 2002. Propylene glycol monomethyl ether occupational exposure. 3. Exposure of human volunteers. Int. Arch. Occup. Environ. Health 75, 203–208. https://doi.org/10.1007/s00420-001-0310-4

Devanthéry, A., Dentan, A., Berode, M., Droz, P.O., 2000. Propylene glycol monomethyl ether (PGME) occupational exposure. 1. Biomonitoring by analysis of PGME in urine. Int. Arch. Occup. Environ. Health 73, 311–315.

Domoradzki, J.Y., Brzak, K.A., Thornton, C.M., 2003. Hydrolysis Kinetics of Propylene Glycol Monomethyl Ether Acetate in Rats in Vivo and in Rat and Human Tissues in Vitro. Toxicol. Sci. 75, 31–39. https://doi.org/10.1093/toxsci/kfg177

Ernst, D.J., 2001. Plastic collection tubes decrease risk of employee injury. MLO. Med. Lab. Obs. 33, 44–46, 48, 50.

European Chemicals Agency (ECHA), n.d. Occupational exposure limits [WWW Document]. URL https://echa.europa.eu/fr/oel (accessed 6.27.19).

Federal Office of Public Health (FOPH), ., n.d. Human biomonitoring projects in Switzerland [WWW Document]. URL www.bag.admin.ch/bag/fr/home/gesund-leben/umwelt-und-gesundheit/chemikalien/chemikalien-im-alltag/human-biomonitoring/human-biomonitoring-projekte-in-der-schweiz.html (accessed 9.30.19).

Food, U.S., Administration (FDA), D., 2001. Guidance for Industry Bioanalytical Method Validation. HttpswwwfdagovfilesdrugspublishedBioanalytical-Method-Valid.-Guid.--Ind.

Fowles, J., Banton, M., Klapacz, J., Shen, H., 2017. A toxicological review of the ethylene glycol series: Commonalities and differences in toxicity and modes of action. Toxicol. Lett. 278, 66–83. https://doi.org/10.1016/j.toxlet.2017.06.009

Fukazawa, T., Yamazaki, Y., Miyamoto, Y., 2010. Reduction of non-specific adsorption of drugs to plastic containers used in bioassays or analyses. J. Pharmacol. Toxicol. Methods 61, 329–333. https://doi.org/10.1016/j.vascn.2009.12.005

Hubner, B., Lehnert, G., Schaller, K.H., Welte, D., Angerer, J., 1992. Chronic occupational exposure to organic solvents. XV. Glycol ether exposure during the manufacture of brakehoses. Int. Arch. Occup. Environ. Health 64, 261–264. https://doi.org/10.1007/BF00378284

Institut national de la santé et de la recherche médicale, (INSERM), 2005. Éthers de glycol : Nouvelles données toxicologiques - Expertise collective. Paris.

Institut national de l'environnement industriel et des risques (INERIS), 2007. Etude des filières de production et d'utilisation des éthers de glycol en France et en Europe. (No. DRC-07-86415-11584A).

Institut National de Recherche et de Sécurité, 2012. Produits chimiques cancérogènes, mutagènes, toxiques pour la reproduction.

Johanson, G., 1988. Aspects of biological monitoring of exposure to glycol ethers. Toxicol. Lett. 43, 5–21.

Johanson, G., Kronborg, H., Näslund, P.H., Byfält Nordqvist, M., 1986. Toxicokinetics of inhaled 2-butoxyethanol (ethylene glycol monobutyl ether) in man. Scand. J. Work. Environ. Health 12, 594–602.

Juenke, J.M., Hardy, L., McMillin, G.A., Horowitz, G.L., 2011. Rapid and specific quantification of ethylene glycol levels: adaptation of a commercial enzymatic assay to automated chemistry analyzers. Am. J. Clin. Pathol. 136, 318–324. https://doi.org/10.1309/AJCPOB9YPQIYKGLJ

Kerrigan, S., 2013. Sampling , storage and stability.. In: Negrusz, A., Cooper, G. (eds). Clarke's Analytical Forensic Toxicology, 2nd edition, chapter 13. Pharmaceutical Press, London, pp. 335–357.

Kratz, A., Stanganelli, N., Van Cott, E.M., 2006. A comparison of glass and plastic blood collection tubes for routine and specialized coagulation assays: a comprehensive study. Arch. Pathol. Lab. Med. 130, 39–44. https://doi.org/10.1043/1543-2165(2006)130[39:ACOGAP]2.0.CO;2

Landry, T.D., Gushow, T.S., Yano, B.L., 1983. Propylene glycol monomethyl ether: A 13-week inhalation toxicity study in rats and rabbits. Fundam. Appl. Toxicol. 3, 627–630. https://doi.org/10.1016/S0272-0590(83)80113-4

Lemazurier, E., Multigner, L., Lecomte, A., Robidel, F., Bois, F.Y., 2003. Ethylene glycol methyl ether (EGME) and alpha isomer of propylene glycol methyl ether (PGME) : two generations of glycol ethers, same adverse effects on reproduction and development. Environ. Risques Santé 2, 89–96.

Livesey, J.F., Perkins, S.L., Tokessy, N.E., Maddock, M.J., 1995. Simultaneous determination of alcohols and ethylene glycol in serum by packed- or capillary-column gas chromatography. Clin. Chem. 41, 300–305.

Moffatt, E.J., Hagardorn, A.N., Ferslew, K.E., 1986. A gas-liquid chromatographic method for quantitation of 1,3-butylene glycol in whole blood or plasma and the separation of the short chain glycols. J. Anal. Toxicol. 10, 35–37.

Morgott, D.A., Nolan, R.J., 1987. Nonlinear kinetics of inhaled propylene glycol monomethyl ether in Fischer 344 rats following single and repeated exposures. Toxicol. Appl. Pharmacol. 89, 19–28.

National Institute for Occupational Safety and Health (NIOSH) 2021. Manual of Analytical Methods (NMAM), 5th Edition.

Palmgrén, J.J., Mönkkönen, J., Korjamo, T., Hassinen, A., Auriola, S., 2006. Drug adsorption to plastic containers and retention of drugs in cultured cells under in vitro conditions. Eur. J. Pharm. Biopharm. 64, 369–378. https://doi.org/10.1016/j.ejpb.2006.06.005

Robertson, O.H., Loosli, C.G., 1947. Tests for the chronic toxicity of propylene glycol and triethylene glycol on monkeys and rats by vapor inhalation and oral administration. J. Pharmacol. Exp. Ther. 91, 52–76.

Sexton, K., L.Needham, L., L.Pirkle, J., 2004. Human Biomonitoring of Environmental Chemicals: Measuring chemicals in human tissues is the "gold standard" for assessing people's exposure to pollution. Am. Sci. 92, 38–45.

Smallwood, A.W., DeBord, K.E., Lowry, L.K., 1984. Analyses of ethylene glycol monoalkyl ethers and their proposed metabolites in blood and urine. Environ. Health Perspect. 57, 249–253.

Starek, A., Miranowicz-Dzieżawska, K., Starek-Świechowicz, B., 2010. Interactive effect of combined exposure to ethylene glycol ethers and ethanol on hematological parameters in rats. Health (N. Y.) 02, 1054–1064. https://doi.org/10.4236/health.2010.29155

Suber, R.L., Deskin, R., Nikiforov, I., Fouillet, X., Coggins, C.R.E., 1989. Subchronic nose-only inhalation study of propylene glycol in Sprague-Dawley rats. Food Chem. Toxicol. 27, 573–583. https://doi.org/10.1016/0278-6915(89)90016-1

Tomicic, C., Berode, M., 2010. Sensitive headspace gas chromatography analysis of free and conjugated 1-methoxy-2-propanol in urine. Anal. Bioanal. Chem. 396, 2709–2714. https://doi.org/10.1007/s00216-010-3487-0

US EPA, O., n.d. Propylene glycol monomethyl ether (PGME) CASRN 107-98-2 | DTXSID8024284 | IRIS | US EPA, ORD [WWW Document]. URL https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=404 (accessed 4.29.21).

Welch, L.S., Schrader, S.M., Turner, T.W., Cullen, M.R., 1988. Effects of exposure to ethylene glycol ethers on shipyard painters: II. Male reproduction. Am. J. Ind. Med. 14, 509–526.

Welsch, F., 2005. The mechanism of ethylene glycol ether reproductive and developmental toxicity and evidence for adverse effects in humans. Toxicol. Lett. 156, 13–28. https://doi.org/10.1016/j.toxlet.2003.08.010

Highlights

- Sampling material impact on glycol ethers concentration in urine and blood
- Urinary PGME and PGBE concentrations are stable in PP material
- Blood PGME and PGBE concentrations are stable in glass material
- Glycol ethers concentration is reduced in PE and PS material
- Biomonitoring samples should be collected in glass for blood and PP for urine