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Abstract

A popular children's arts and crafts toy made international headlines when it was discovered that 1,4-butanediol had been substituted into some of its formulations. The chemical 1,4-butanediol rapidly converts to the date-rape drug γ-hydroxybutyric acid (GHB) upon ingestion and resulted in the accidental poisoning of some children. In this experiment, students extract 1,4-butanediol from commercially available toy beads (or prepared simulations) using their knowledge of pharmaceutical chemistry, solubility, etc. Using case studies available in the literature, students develop a quantitative analysis experiment for 1,4-butanediol extracted from the toy beads and, through approximation, relate the extractable amount of 1,4-butanediol to dose-response data for GHB. In this way, student learning is linked to current events, making routine analyses relevant and engaging.

Introduction

The *Medical Journal of Australia* reported a Notable Case involving the accidental poisoning of two children from ingestion of toy beads. The popular children's art toys were manufactured in Hong Kong and purported to contain the relatively harmless 1,5-pentanediol. However, the toys had been manufactured with the potentially fatal 1,4-butanediol, a chemical that rapidly converts in the body to the date-rape drug GHB (Figure 1). [1] 1,4-Butanediol is widely available as an industrial chemical and legal in products “not intended for human consumption”. [2] Because of this, abusers can obtain 1,4-butanediol and other GHB analogs and precursors legally. However, consumption or distribution of these compounds is illegal. The substitution from 1,5-pentanediol to 1,4-butanediol may have been accidental or perhaps driven by financial goals. The price of 1,4-butanediol is between about $1,350-2,800 per metric ton, while the price for 1,5-pentanediol is about $9,700 per metric ton. [3] This substitution resulted in the accidental poisoning of some children, prompting numerous news stories and a world-wide recall of the product.

Experimental

1,4-Butanediol calibration standards (CAS# 110-63-4) were prepared in acetone and analyzed using a Shimadzu GC-17A Gas Chromatography (GC) system with a SS420x Flame Ionization Detector (FID) and a Rtx®-5 column (Restek 15m, 0.25mm I.D., 0.25µm Cat. 10220) (Figure 2). GC-FID parameters were set with an initial temperature of 90ºC for 1.5 min ramped at 10ºC/min to a final temperature of 110ºC in split injection mode with inlet and detector temperatures at 250ºC. A calibration curve was constructed and shows linear response for 1,4-

butanediol standards (Figure 3). Single toy beads (Bindeez, also marketed as Aqua Dots) [1] were sealed in Teflon-capped vials and swelled overnight in acetone and the resulting extract was filtered using a 0.45µm nylon filter syringe and quantitatively transferred to a 10-mL volumetric flask, diluted to volume, and analyzed by GC-FID. The product containing 1,4-butanediol may not be readily available to instructors in which case simulations using currently marketed product (Pixos) containing 1,2,3-propanetriol may be used as a substitute. Alternatively, instructors may spike 1,4-butanediol onto any commercially available plastic bead.

Results and Discussion

GHB is available as the pharmaceutical sodium oxybate (Xyrem) and marketed as a narcolepsy medication. Therefore, suggested therapeutic dosages for sodium oxybate for an adult patient are available (2250 mg) and can be used in calculations of dose/response for ingestion of 1,4-butanediol. [4] Using an average experimental mass 1,4-butanediol extracted from the toy beads (5.155 mg/bead), students can calculate the number of beads needed to produce a therapeutic response for GHB (Equation 1) in an adult assuming that the 1,4-butanediol converts 100% to GHB [1].

$$\text{Equation 1: } 2250 \text{ mg 1,4-butanediol} \times \frac{1 \text{ toy bead}}{5.155 \text{ mg 1,4-butanediol}} \approx 436 \text{ beads}$$

Assuming the average mass of an adult male is 89 kg and a 2-year old child is 13 kg [5], students can approximate the therapeutic dose for the child in The Medical Journal of Australia case study [1] using the proportionality in Equation 2.

Equation 2:

$$\frac{\text{2250 mg 1,4-butanediol therapeutic adult dose}}{\text{89 kg average adult}} \approx \frac{\text{329 mg 1,4-butanediol therapeutic child dose}}{\text{13 kg average 2 year old child}}$$

Gunja, *et al.* document case reports of a 2-year old boy and 10 year old girl who were admitted to hospitals in the winter of 2007. Both were in a comatose state and pathology confirmed the presence of 1,4-butanediol in the urine. Tests later confirmed that the source of the accidental poisoning was ingestion of the toy beads. Using the case studies available in the literature, students can develop a quantitative analysis experiment to extract 1,4-butanediol from the toy beads and, through approximation, relate the extractable amount to number of beads capable of producing a therapeutic response in an average 2 year old child (Equation 3).

Equation 3: $\text{329 mg 1,4-butanediol} \times \frac{\text{1 toy bead}}{\text{5.155 mg 1,4-butanediol}} \approx \text{64 beads}$

After the international recall, new formulations for the toy craft bead were launched. [6] The fundamental difference was the substitution of 1,5-pentadiol (and accidental poison 1,4-butanediol) with glycerol (1,2,3-propanetriol). The experiment is readily adaptable as a simulation to determine the amount of glycerol present on commercially available toy craft beads and calculate the therapeutic dosage if glycerol simulant (Pixos) were assumed to be 1,4-butanediol (Bindeez or Aqua Dots).

Conclusion

Students are able to determine the average percent weight of 1,4-butanediol in the toy craft bead, and based on the percent weight (approximately 7% w/w), calculate the hypothetical therapeutic doses for published average patient demographics. Case studies in the existing literature allow students to expand knowledge gained in laboratory to dose-response data in real case studies of accidental poisoning. Simulations using toy craft beads that are currently commercially available make this experiment accessible to all undergraduate chemistry programs. Additional experiments using volumetric analysis are in process and may allow adoption of this experiment in general chemistry.

Acknowledgements

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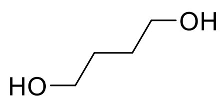
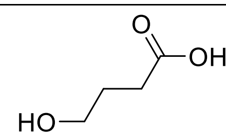
1,4-Butanediol	Alcohol Dehydrogenase → Aldehyde Dehydrogenase	γ-Hydroxybutyric Acid
		

Figure 1. Bioconversion of 1,4-butanediol to γ-hydroxybutyric acid by alcohol and aldehyde dehydrogenases.

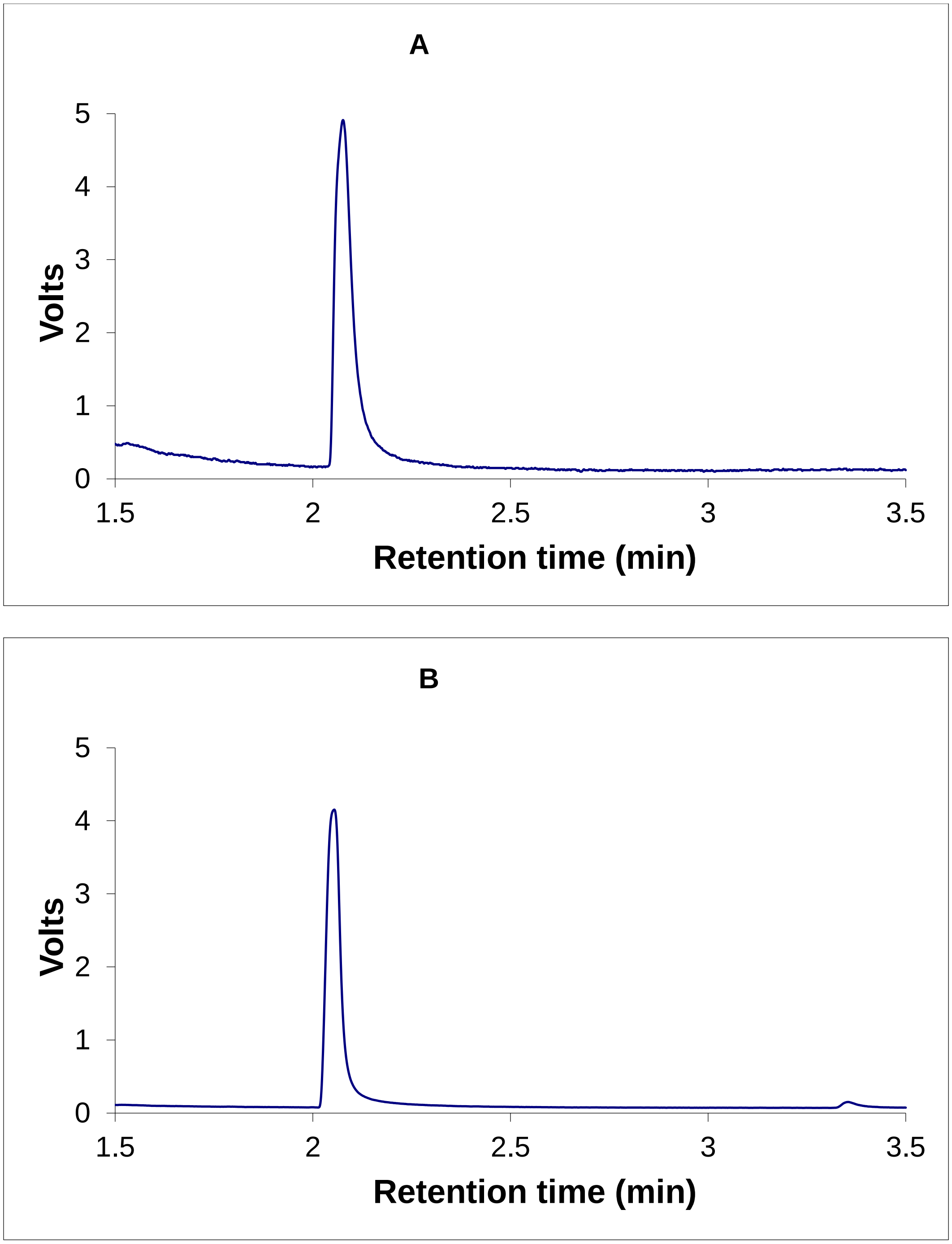


Figure 2. (A) GC-FID analysis of 100 ppm stock solution of 1,4-butanediol in acetone, and **(B)** extract from a single toy bead swelled overnight in acetone.

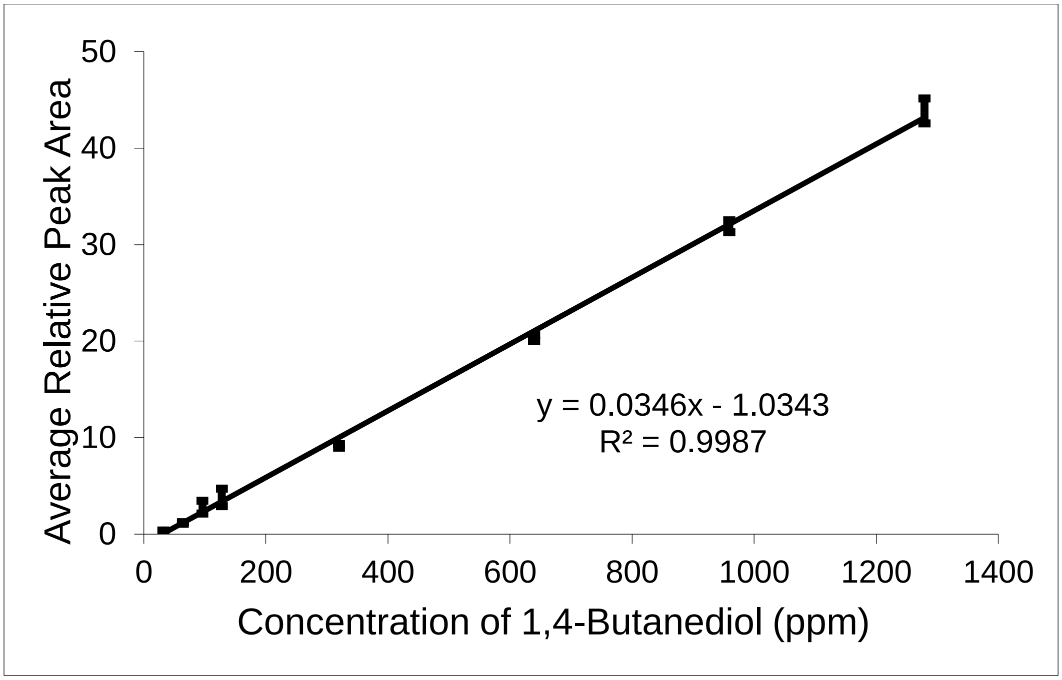


Figure 3. Representative student generated calibration curve.