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Article

Quantifying Zinc Contamination from Laboratory Syringes

Sarah G. Lindgren [1], Laura J. Sakol [2], Monica Hoover [3], Timothy M. Raymond [1] and Dabrina D. Dutcher [1,2,*]

[1] Department of Chemical Engineering, Bucknell University, Lewisburg, PA 17837, USA; sgl012@bucknell.edu (S.G.L.); traymond@bucknell.edu (T.M.R.)
[2] Department of Chemistry, Bucknell University, Lewisburg, PA 17837, USA; ljs034@bucknell.edu
[3] Environmental Engineering & Science Laboratory, Bucknell University, Lewisburg, PA 17837, USA; mah047@bucknell.edu
* Correspondence: dabrina.dutcher@bucknell.edu

Abstract: While many sources of contamination in chemical and biological laboratories are well understood and known, some are less so. To quantify the magnitude of the potential contamination of solutions by zinc in common laboratory syringes, a study was conducted on solutions stored in rubber-containing syringes in which the rubber was catalyzed by zinc. This study identified specific factors contributing to contamination from laboratory syringes, including the syringe brand, time, solution type, and pH. Two common syringe brands, Covidien and BD, were tested, and three time durations, 0 days, 1 day, and 14 days, were examined. The solutions tested included sucrose and tartaric acid, representing both covalent and ionic species. Additionally, this study employed a pH range of 2 to 13 to further explore zinc contamination across a wide range of conditions and factors. The zinc concentration from the syringes was measured using inductively coupled plasma mass spectrometry (ICP-MS). The results, which ranged from less than 20 to over 600 μg L^{-1}, revealed increased zinc concentration at both extreme pH values, while remaining lower but measurable at neutral pH levels. Zinc contamination is important to study because its contamination in laboratory syringes could interfere with the detection of other elements, further skew laboratory data, unexpectedly catalyze reactions, and lead to inconsistencies in experimental conditions. This study further emphasizes the broader significance of understanding pollutants within laboratory settings. The findings highlight the intricate dynamics of zinc contamination, stressing the need for the control of environmental factors and the broad dissemination of lesser-known sources. Recognizing the potential impact of contaminants like zinc is crucial, as it not only influences analytical accuracy, but also mirrors the wider concern of pollutants compromising scientific integrity in diverse experimental conditions.

Keywords: rubber; zinc; laboratory pollutant; syringe

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1. Introduction

In January 2021, *Nature Catalysis* published a paper claiming to execute a highly desired metal-free coupling reaction. However, upon further investigation, it was discovered that the reaction contained trace amounts of palladium, and the paper was deemed flawed and had to be retracted. Even the most meticulous techniques can yield inaccurate results if contamination from the equipment is unknowingly present. However, this is not the first instance in which the scientific community debunks claims of metal-free chemistry [1]. Additionally, zinc supplementation in cell culture media can vary from zinc-free to 0.7 pM in Wiliams E Media to 3 nM in Han's Nutrient Media ([2] Millipore Sigma, Burlington, MA, USA). Unknowing alterations in these concentrations could lead to incorrect experimental results or interpretations.

These cases highlight the importance of understanding the sources of contamination in the lab. Syringes are a commonly used laboratory supply; approximately six billion syringes are produced worldwide annually, with 663 million manufactured in the US alone [3,4], making syringes a logical place to study zinc contamination. This paper explores the contamination of solutions stored in syringes with zinc-catalyzed rubber plungers.

The previous example of contamination highlights the significance of understanding sources of contamination and potential pollution in the laboratory setting. The rubber vulcanization process is catalyzed with zinc, so the black rubber on the syringe plunger has been identified as the source of zinc [5]. Despite its relevance, there is a dearth of academic literature documenting the zinc concentration in syringes, leaving this contamination unquantified and poorly known. In a study on the contamination from syringes and blood container pots, Taylor and Marks [6] found that substantial amounts of zinc in unpredictable levels were leached from the rubber end cap on disposable plastic syringes. In the 50 years since Taylor and Mark's study, there have been changes in the rubber vulcanization and manufacturing processes, so an updated investigation of zinc contamination of laboratory syringes is warranted. Additionally, Taylor and Mark's study did not identify specific factors that contribute to varying zinc concentrations nor quantify the levels of zinc contamination. Consequently, limited knowledge exists regarding the extent and control of this contamination, which is cause for concern given the ubiquity of syringes in the scientific industry.

Though rubber is problematic, the absence of rubber compromises the syringe's ability to supply a tight seal. Rubber plungers with "higher zinc extractables" are known to potentially interact with the syringe's contents, resulting in undesirable "aggregates" [7]. To assess its suitability for specific applications, syringe manufacturers can perform a "forced extraction study" on the rubber plunger. The contamination is poorly documented, indicating a lack of awareness of zinc contamination within the scientific community. Consequently, the extent of zinc contamination in rubber-containing syringes and the factors that affect contamination remain unknown.

Inductively coupled plasma mass spectrometry (ICP-MS) is the preferred method for quantifying low concentrations of atomic elements in a sample, including zinc, due to its sensitivity and widespread use [8]. ICP-MS measures most of the elements in the periodic table at low concentrations (µg L^{-1}) and ultra-low concentrations (ng L^{-1}), with a few exceptions [9,10].

In this experiment, we focused on several factors: the syringe brand, ionic vs. covalent solutions, duration of solution exposure, and solution pH, which are highlighted in Figure 1 as a geometrical representation. Both sucrose and tartaric acid are organic compounds, one predominantly covalent and one predominantly ionic, compatible with ICP-MS analysis, and are relatively innocuous in laboratory settings. The objective was to identify and quantify the factors contributing to the highest extraction of zinc from the rubber plunger.

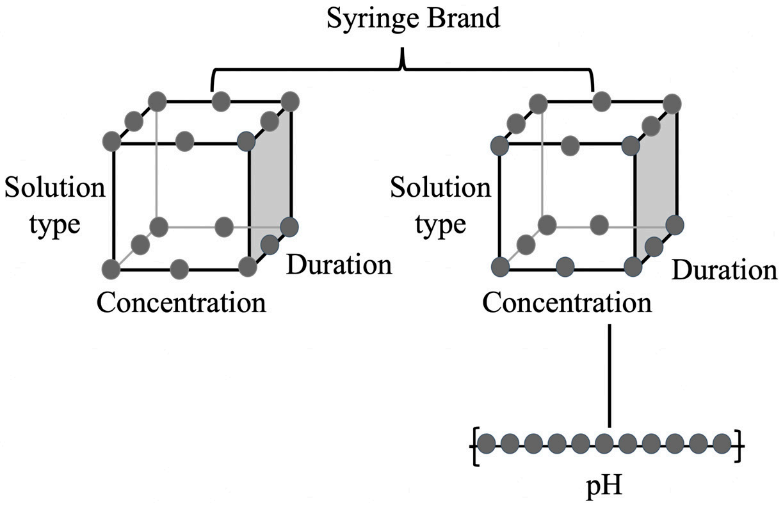

Figure 1. A geometric experimental diagram categorizing the different factors examined that may lead to the leaching of zinc from laboratory syringes.

2. Material and Methods

The experimental materials utilized are presented in Table 1.

Table 1. Supplier and lot numbers for experimental materials.

Item	Supplier	Lot Number (s)
Covidien 60 mL Luer-Lok syringe	VWR (Radnor, PA, USA)	027252X
BD 50 mL Luer-Lok syringe	VWR (Radnor, PA, USA)	1145497 and 1215381
Norm-Jet 60 mL Luer-Lok syringe *	VWR (Radnor, PA, USA)	20 I 18 0 B
Sucrose	VWR (Radnor, PA, USA)	20G1356994
L-tartaric acid	VWR (Radnor, PA, USA)	19J1056043
25 mm 0.45 µm nylon membrane Syringe filter	VWR (Radnor, PA, USA)	10163004A
15 mL PP centrifuge tubes	VWR (Radnor, PA, USA)	21024058
Multi-element standard solution	Inorganic Ventures (Christiansburg, VA, USA)	P2-MEB682937
Ultrapure water (18 MΩ)	Veolia (Aubervilliers, France)	N/A
Sodium hydroxide	VWR (Radnor, PA, USA)	Bulk
Nitric Acid—low metals	Aristar Plus/VWR (Radnor, PA, USA)	1121050

* Rubber free-syringe.

2.1. Solution Preparation

Prior to preparing the solutions, all pre-cleaned glassware used to make the solutions was washed with a 1% nitric acid solution three times and rinsed with ultrapure water three times to avoid introducing any unwanted compounds to the samples and the ICP-MS. Sucrose and tartaric acid were each dissolved with ultrapure water in 1.0 L volumetric flasks to create the desired solutions.

The solutions intended for the various pH levels were mixed with sodium hydroxide and nitric acid. The solutions were mixed, and then a sample from each solution was removed to be tested for pH to confirm that all solutions were within 0.2 pH units of the target pH.

Before filling the experimental syringe with a given solution, the sample was filtered using a zinc-free control syringe (Norm-Jet brand) and a 0.45 µm Nylon syringe filter (Table 1). The control syringe did not contain a rubber plunger and, instead, was composed solely of polypropylene to avoid introducing external zinc to the samples. Laboratory blanks confirmed the absence of other sources of zinc.

2.2. Solution Exposure (in Syringe)

Different durations of solution containment in the syringe were tested to determine if the longer the solution was contained in the syringe, the more zinc would be leached. Sample preparation occurred in three phases, in line with the three durations tested in this experiment. The 14-day samples were prepared two weeks before the scheduled ICP-MS run date. Similarly, the 1-day samples were prepared the day before the run, and the 0-day samples were prepared on the day of the ICP-MS run. The 0-day samples were contained in the syringes for less than a minute. During the exposure times, all the syringes were stored with the rubber stopper down, maximizing interaction between the solutions and the stoppers. All samples added to the syringes were 10.00 ± 0.02 mL. Each syringe was capped with a 0.45 µm syringe filter to reduce the evaporation of the solutions.

Two samples were prepared for each solution described in the cubes in the geometric experimental diagram (Figure 1), and replicates were analyzed. Two syringe brands, Covidien and BD, were tested.

The BD syringes were found to have leached a significant amount of zinc and were further tested using an additional twelve samples, produced at integer values on the pH scale (*vide supra*) which were stored in the rubber-containing syringes for 14 days prior to running through the ICP-MS. The solutions were moved into pre-rinsed 15 mL sample tubes at the end of the exposure duration.

After the designated time duration elapsed for each sample, during which each sample was intentionally not agitated while sitting, the solutions in the syringes were analyzed immediately by ICP-MS [11]. The samples were dispensed into 15 mL pre-rinsed centrifuge tubes from their respective syringes. Each centrifuge tube was rinsed thrice with a 1% nitric acid solution before introducing the samples. All samples, including blanks, were diluted to achieve a final concentration of 1% nitric acid in accordance with the standard ICP-MS procedure. Nitric acid was chosen as the preferred acid due to its minimal interference with polyatomic species [12]. Standard solutions with 1, 10, 100, and 250 μg L^{-1} zinc concentrations were created in a 1% nitric acid solution in a procedure similar to the test solutions, but they were never exposed to rubber.

Nitric acid and sodium hydroxide were used to create a pH range of 2 to 13. The sample pH's were confirmed through pH electrode analysis. After collecting samples in the 2 to 13 pH range and transferring them into centrifuge tubes, they were subsequently placed into BD syringes and allowed to sit for 14 days in contact with the rubber plunger. Following this equilibration period, the samples were analyzed by ICP-MS.

3. ICP-MS Methods

Most interferences in ICP-MS are attributed to polyatomic interferences in mass spectrometry, where atomic or molecular ions with the same mass-to-charge ratio as the compounds of interest can cause interference. To address this issue, the ICP-MS software includes measures to avoid interferences caused by overlapping isotopes of different elements, known as atomic "isobaric" interferences [13]. To deal with isobaric interferences, we monitored Zn^{66} because it has fewer known interferences [8,13–22]. The ICP-MS operating parameters are shown in Table 2.

Table 2. Thermo-Fischer i-CAP RQ ICP-MS operating parameters.

ICP-MS Plasma	Parameters
Instrument Parameters	
RF power	1550 W
Plasma power	1550 W
Auxiliary gas flow	0.80 L min^{-1}
Nebulizer gas flow	1.04 L min^{-1}
Sampling depth	5 mm
Sample/skimmer diameter orifice	Nickel cones/3.5 mm insert
Acquisition parameters	
Scanning mode	KED
Dwell time	0.01 s
Sampling flow	20 rpm
Replicate count	15
Integration mode	Peak area
Isotopes	^{64}Zn, ^{66}Zn, and ^{68}Zn

4. Results

The factors tested in this experiment were solution type, syringe brand, time, and pH. Two solutions, sucrose and tartaric acid, were tested for the solution type. Two brands were examined: Covidien and BD. For the time factor, three levels were examined: 0 days, 1 day, and 14 days. The pH levels tested were 2 to 13, using sodium hydroxide and nitric acid to adjust the pH of ultrapure water.

4.1. Factor: Solution Type/Concentration

The sucrose and tartaric acid samples underwent the same number of measurements under the same conditions. The samples captured in Figure 2 are subject to different syringe types, solution concentrations, and times. This experimental design still allows for comparison but will result in broader data distributions [23]. Consequently, a high level of variability is expected, so the spread of the data should be interpreted appropriately. Figure 2 represents all the factors compared to each other, showing higher levels of zinc extraction overall for BD syringes after a 14-day duration.

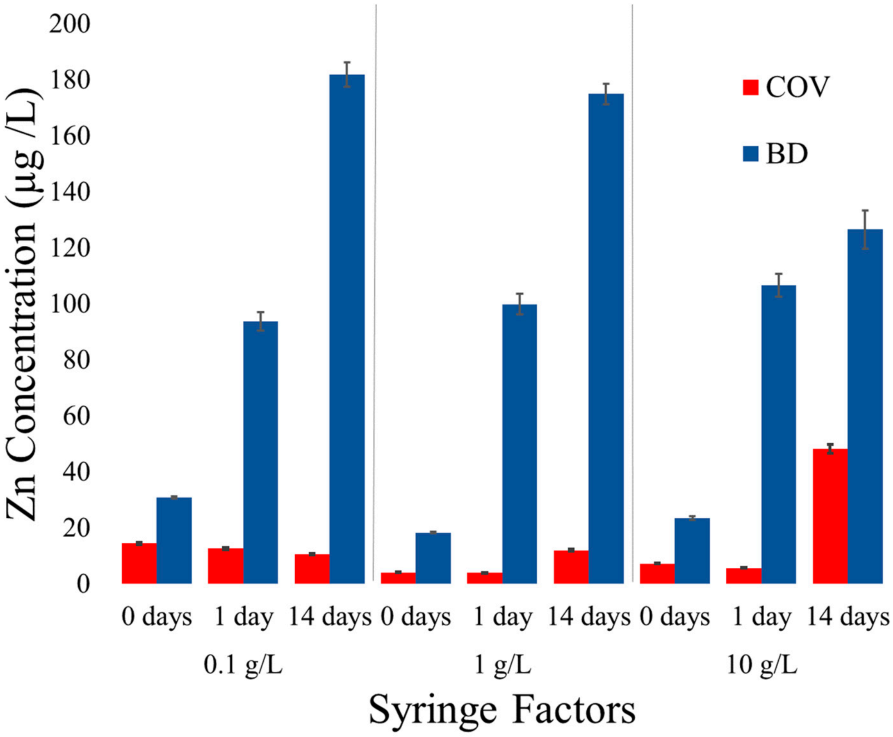

Figure 2. Time and concentration in BD and Covidien syringes in μg L^{-1}. Zinc contamination is detected at every concentration and designated duration. The error bars represent 3 standard deviations.

As anticipated, the tartaric acid samples generated the greatest zinc concentration due to tartaric acid's structure and the higher concentration of reactive hydronium ions available to extract the zinc [24], as seen in Figure 3. Error bars are not included here as the values represented are averaged over all of the included factors and levels, and thus would not be meaningful [23]. This observation prompted further investigation into the influence of pH values, as pH is the interplay of solution concentration. The varying concentrations (0.1, 1, and 10) in grams per liter (g/L) were also subjected to different syringes and durations, resulting in a wide range of variability. A difference in zinc concentration between the two syringe brands suggests that the two brands are likely using different rubber formulations. The 14-day samples generated the next highest average zinc concentration of 95 μg L^{-1}. It is logical that the longer the samples were contained in the syringe, the more zinc was extracted, as there was more time for the samples to interact with the rubber zinc source. The BD samples followed closely behind the 14-day samples, with an average zinc concentration of 93 μg L^{-1}. The highest zinc concentration was extracted when a BD syringe was filled with a solution for 14 days. The maximum zinc concentration extracted from a syringe was 670 μg L^{-1}, a potentially concerning concentration in some circumstances.

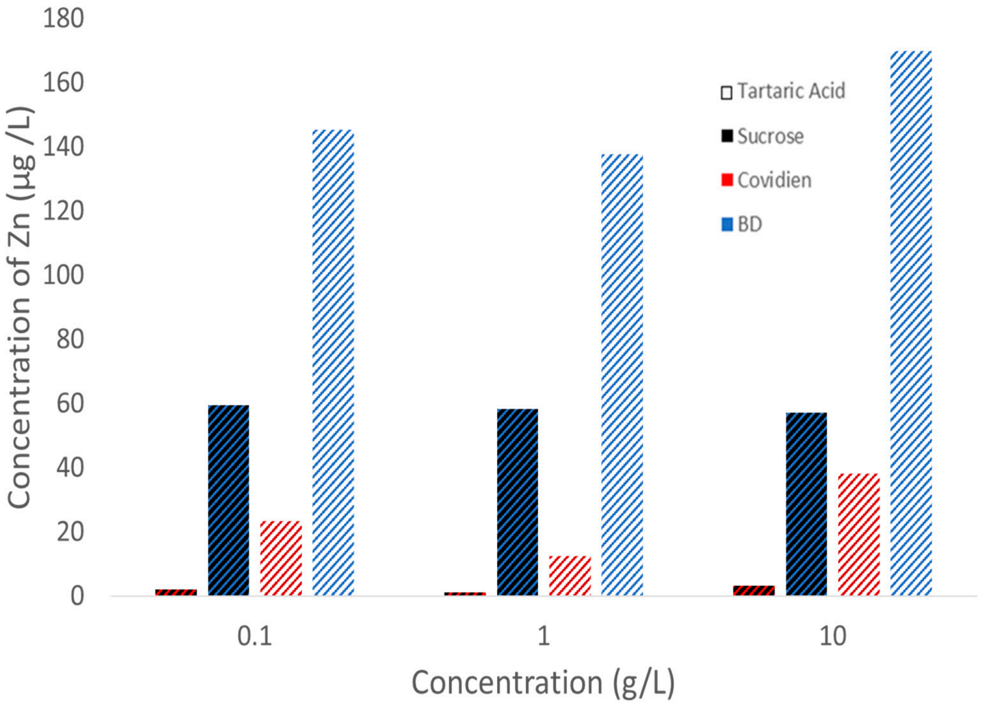

Figure 3. Tartaric acid and sucrose in BD and Covidien syringes. Zinc contamination in the solutions is detected and measured at each concentration level in µg L^{-1} in both Covidien and BD syringes. The two colors represented in the striping of the bars represent the manufacturer and type of solution used (shown in the legend).

4.2. Factor: Syringe Brand

Figure 2 indicates that more zinc was leached from the BD syringes than from the Covidien syringes overall. This result indicates that the syringe brand affected the zinc concentration. The syringe brand had the greatest effect on the 14-day samples and did not have a statistically significant impact on the 0-day samples.

The BD syringes experienced an increase in zinc concentration as time increased for all solutions. The more time a solution spent in the syringe, the more zinc was dissolved as there was more contact between the solution and the rubber.

The extreme predictability of the BD syringes creates a false expectation for the Covidien syringes. In general, the zinc concentration of the Covidien samples remains relatively constant compared to the BD syringe. All samples leached a measurable amount of zinc when in the BD syringes. A difference in zinc concentration between the two syringe brands suggests that the two brands are likely using different rubber formulations. Some variability between syringe brands was anticipated, hence the inclusion of syringe brand as a factor to be tested.

The largest zinc concentration was extracted after 14 days for both syringe brands. The zinc concentration extracted from the BD syringes ranged from 98 to 110 µg L^{-1} compared to 7 to 21 µg L^{-1} for the Covidien syringes.

4.3. Factor: Time

As time increases, there is a corresponding rise in zinc concentration. The bar graph in Figure 2 shows a noticeable upward trend in zinc concentration over time for BD syringes, as opposed to Covidien syringes. Notably, the measurements of zinc concentration in the BD syringes show a wider range of Zn concentrations compared to those of the Covidien syringes.

In the case of the Covidien syringes, there is a notable stability in zinc concentration as time progresses. This trend is shown in the bar graph (Figure 2), which consistently shows relatively low zinc concentration levels at each duration examined. Figure 2 illustrates the average zinc extracted during the different extraction durations while also highlighting the lack of substantial variations in zinc concentration over time for Covidien syringes. Conversely, the BD syringes demonstrate significant leaching of zinc compared to the Covidien samples at each time duration.

The graph (Figure 2) provides evidence of an increase in zinc concentration as time progresses, regardless of the solution type. The longer the rubber plunger was immersed in the acid, the greater the extent of zinc extraction observed. Logically, the most acidic and basic samples exhibit the widest range of zinc concentrations, as they correspond to the highest concentration of hydronium ions.

In summary, Figure 2 highlights the influence of time on zinc concentration in BD syringes, further confirming its impact. Time does not have a similar effect on zinc concentration in Covidien syringes, suggesting a potential disparity in the uniformity of the rubber material used in the syringes.

4.4. Factor: pH

The effect of pH is most significant in the case of the 14-day samples, particularly for pH levels of 2 and 13, as evidenced by Figure 4, which shows BD syringes on a pH scale from a 14-day duration. The duration, combined with the higher concentration of hydronium ions, led to higher zinc concentrations. It makes sense that the more time a solution spent in the syringe, the more zinc was extracted, as there was prolonged contact between the rubber material and the reactive hydronium/hydroxide ions.

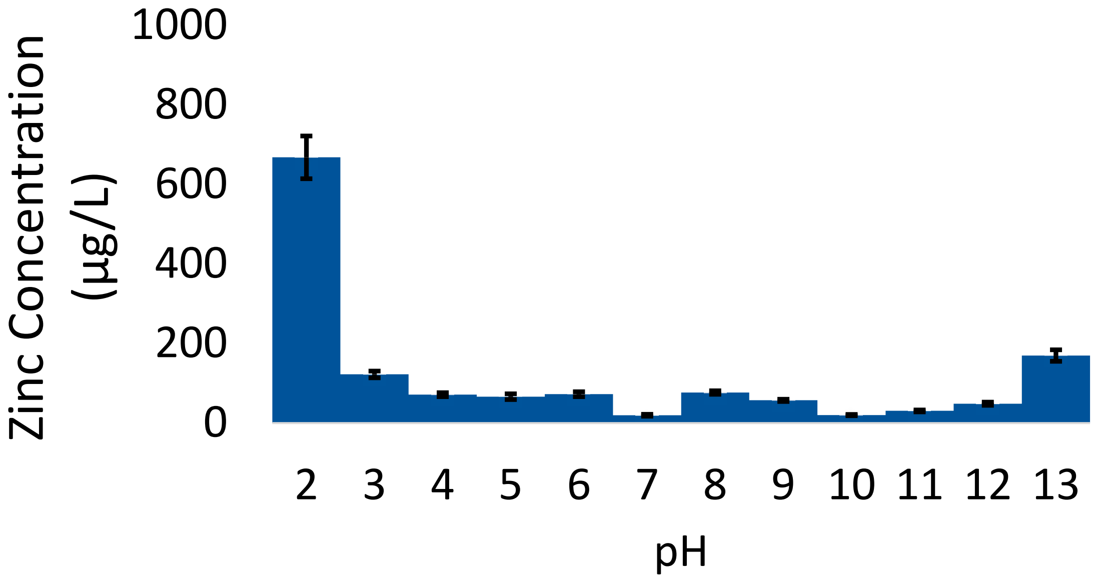

Figure 4. The average zinc concentration extracted from BD syringes at different pH levels is depicted for a 14-day duration, showing an increase in zinc concentration at the pH extremes. Each data point represents the average zinc concentration of all samples corresponding to a specific pH value produced from either nitric acid or sodium hydroxide. The error bars represent three standard deviations.

Figure 4 examines the effect of pH on zinc extraction. The relationship between pH and zinc concentration makes sense as the solution environment becomes more reactive with elevated hydronium concentrations and can leach more zinc from the rubber. The extraction of zinc can be an acid-driven process. It follows that the most acidic solution with the highest concentration of reactive hydronium ions extracted the most zinc. Tartaric acid, a dicarboxylic acid, is a stronger cross-linker than monocarboxylic acids due to hydrogen bond formation [25]. The carboxylic acid functional group binds strongly to divalent metals [18,26], which might lead to a more stabilized form of zinc in the solution.

Ultimately, pH had a more significant impact on the BD syringes in terms of zinc concentration than the Covidien syringes. Therefore, a range of pH values were tested in the BD syringes.

5. Discussion and Conclusions

We quantified the amount of zinc extracted from syringes stored under typical laboratory conditions and determined some factors that affected the amount extracted. The examined factors, represented in Figure 2, were the syringe type, solution type, solution concentration, pH, and time. Zinc concentration increased at the extreme pH levels, as the duration increased, and when the solution was contained in a BD syringe. Below, the factors are ranked by the power of the factor analyzed from highest to lowest:

1. pH;
2. Syringe brand;
3. Time;
4. Solution type and concentration.

The results indicate the necessity of choosing the correct syringe type (with or without a rubber stopper) depending on the sensitivity of the experiment to zinc. It also suggests that solutions should not be stored in rubber-containing syringes, especially if the pH of the solution is extremely acidic.

The results of this experiment speak to the importance of understanding sources of contamination in the laboratory; the elevated zinc concentrations observed under extreme pH levels and prolonged storage times signify potential risks of pollutant interference in experimental analyses. Even low levels of contamination can yield inaccurate results, and contamination can be introduced in a variety of unsuspected ways.

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