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Chlorine Isotopic Composition of Perchlorate in Human Urine as a Means of Distinguishing Among Natural and Synthetic Exposure Sources

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Abstract

Perchlorate (ClO_4^-) is a ubiquitous environmental contaminant with high human exposure potential; it has both natural and man-made sources in the environment. Natural perchlorate forms in the atmosphere from where it deposits onto the surface of Earth, whereas synthetic perchlorate is manufactured as an oxidant for industrial, aerospace, and military applications. Perchlorate exposure can potentially cause adverse health effects in humans by interfering with the production of thyroid hormones through competitively blocking iodide uptake. To control and reduce perchlorate exposure, the contributions of different sources of perchlorate exposure need to be quantified. Thus, we demonstrate a novel approach for determining the contribution of different perchlorate exposure sources by quantifying stable and radioactive chlorine isotopes of perchlorate extracted from composite urine samples from two distinct populations: one in Atlanta, USA and one in Taltal, Chile (Atacama region). Urinary perchlorate from the Atlanta region resembles indigenous natural perchlorate from the southwestern USA [$\delta^{37}\text{Cl} = +4.1 \pm 1.0 \text{ ‰}$; $^{36}\text{Cl}/\text{Cl} = 1811 (\pm 136) \times 10^{-15}$], and urinary perchlorate from the Taltal, Chile region is similar to natural perchlorate in nitrate salt deposits from the Atacama Desert of northern Chile [$\delta^{37}\text{Cl} = -11.0 \pm 1.0 \text{ ‰}$; $^{36}\text{Cl}/\text{Cl} = 254 (\pm 40) \times 10^{-15}$]. Neither urinary perchlorate resembled the isotopic pattern found in synthetic perchlorate. These results indicate that natural perchlorate of regional provenance is the dominant exposure source for the two sample populations, and that chlorine isotope ratios provide a robust tool for elucidating perchlorate exposure pathways.

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INTRODUCTION

Perchlorate (ClO_4^-) is a highly oxidized anion and is a widespread contaminant that when ingested can potentially cause adverse health effects in humans. Once in the body, perchlorate can competitively block iodide from entering the thyroid, potentially affecting further production of thyroid hormones. Deficiency of thyroid hormones has severe health effects especially for fetuses, infants, and young children. Because the thyroid hormones are crucial for neurodevelopment in the early stages of life, their deficiency can cause irreversible impairment in the nervous system, particularly in the brain.¹⁻⁵

Perchlorate has been detected in surface water and groundwater across the United States⁶⁻¹⁴ as well as in a wide range of food products including milk, infant formulas, fruits, and vegetables.¹⁵⁻²¹ The primary routes of perchlorate exposure to humans appear to be through oral intake of food and drinking water.²¹⁻²⁵ Perchlorate has been detected in human U.S. breast milk^{16, 26-28} and all urine samples tested as part of the National Health and Nutrition Examination Surveys between 2001 and 2008^{22,29, 30} indicating widespread human exposure across the United States. Urinary perchlorate is an indicator of exposure since perchlorate is not metabolized and exits the body primarily through urine.³¹ Children are exposed to significantly higher doses of perchlorate compared with adults, likely because of higher rates of consumption of foods that tend to contain higher perchlorate levels.^{21, 32, 33}

Perchlorate originates from different natural and manufactured sources that can be distinguished by their relative isotopic signatures based on the stable chlorine isotope ratios reported in the conventional delta (δ) notation and on $^{36}\text{Cl}/\text{Cl}$ ratios. Perchlorate that forms in the atmosphere deposits onto the surface of Earth, but it accumulates mainly in dry regions such as the Atacama Desert in Chile and the Death Valley in the United States.³⁴⁻⁴⁰ Two main types of isotopically distinct natural perchlorate have been measured to date: one type having generally positive $\delta^{37}\text{Cl}$ values (0 to +6 per mil) combined with relatively high $^{36}\text{Cl}/\text{Cl}$ ratios ($3,000 \times 10^{-15}$ to $29,000 \times 10^{-15}$) has been found at locations across the United States and in Namibia, United Arab Emirates, China, and Antarctica; and the second type characterized by anomalously low $\delta^{37}\text{Cl}$ values (-20 to -10 per mil) and relatively low $^{36}\text{Cl}/\text{Cl}$ ratios (22×10^{-15} to 590×10^{-15}) has been found only in the Atacama Desert of northern Chile.^{10, 41, 42} Atacama perchlorate is associated with nitrate-rich caliche deposits and is by far the largest known reservoir of natural perchlorate on Earth.^{8, 34, 43, 44}

Substantial quantities of Atacama perchlorate were introduced into the environment across the United States during the first half of the 20th century due to the widespread application of imported Chilean nitrate fertilizer.^{35, 45-47} Synthetic perchlorate is primarily used as an oxidant in a variety of solid rocket propellants and explosives as well as in consumer products including fireworks, matches, air bags, chlorine bleach, safety flares, and chlorate herbicides.^{9, 48-50} The isotopic composition of synthetic perchlorate is distinctly different from both types of natural perchlorate in its relatively consistent $\delta^{37}\text{Cl}$ value ($+0.6 \pm 1.0$ per mil) and its low $^{36}\text{Cl}/\text{Cl}$ ratio (1×10^{-15} to 40×10^{-15}).^{10, 42, 51}

Recent studies evaluated dietary sources of perchlorate in the United States by estimating overall perchlorate contribution to the food chain from all potential sources⁴⁵ or by using quantities of perchlorate in different food products, drinking water, and urine.^{21, 22} However,

none of these studies can differentiate between indigenous natural perchlorate, natural Atacama perchlorate, and synthetic perchlorate as the primary source of perchlorate exposure. The objective of this study was to identify the exposure source of perchlorate by measuring the chlorine isotopic composition ($\delta^{37}\text{Cl}$, $^{36}\text{Cl}/\text{Cl}$) of perchlorate extracted from urine. This novel approach can distinguish between natural and anthropogenic sources of perchlorate as the primary source of perchlorate exposure. We hypothesized that the chlorine isotopic composition of urinary perchlorate would resemble that of groundwater, surface water and soil in the geographical region of the population.

MATERIALS AND METHODS

Sample Collection

Perchlorate was extracted from composite urine samples for isotopic analysis by using 100 cm³ clear PVC columns filled with Purolite A530E bifunctional anion exchange resin. This resin is exceptionally selective for perchlorate,⁵²⁻⁵⁴ and similar columns have previously been used to extract perchlorate from groundwater.^{11-13, 41, 55} Detailed description of sampling column design and isotopic analytical procedures are given by Hatzinger et al. (2011)⁵⁶. The first perchlorate sample was extracted from a total volume of 40 L urine pooled from ~133 anonymously collected urines from residents of the Atlanta metro area over a two week collection period. The second sample was extracted from a total volume of 1.05 L urine pooled from 49 clinical residual urine samples collected from adult residents of Taltal, Chile (Atacama region). Human specimen use was in accordance with human subjects review (University of California Berkeley and Pontificia Universidad Católica de Chile).

After sampling was completed, the resin columns were shipped to the Environmental Isotope Geochemistry Laboratory at the University of Illinois at Chicago in a cooler filled with ice packs, and the sample columns were kept refrigerated until analysis.

Perchlorate concentrations in urine samples were determined before and after the Purolite columns using ion chromatography tandem mass spectrometry (IC-MS/MS)⁵⁷ at CDC. Aliquots were run in triplicates for each composite sample. The amounts of perchlorate retained on each column and the final yields of purified perchlorate were independently determined, and the estimates agreed well for both perchlorate samples (Table 1).

Extraction of perchlorate from the resin columns was performed using procedures described by Hatzinger et al. (2011)⁵⁶. Briefly, the resin was ultrasonically cleaned in deionized water, and then it was flushed with 4M HCl to remove common anions including organic acids. Subsequently, perchlorate was eluted with 1M FeCl₃-4M HCl,⁵⁴ and iron was removed by passing the diluted eluant through a cation exchange resin, then the iron-free solution was evaporated to ~2 mL volume. The final purification of perchlorate was performed by chromatography, then perchlorate was precipitated and recrystallized as tetra-n-pentylammonium perchlorate (TPAClO₄).⁵⁸ The overall sample processing blank for perchlorate was 5 µg, which was less than 5% of the perchlorate recovered for isotopic analysis.⁵⁹

SIMS Measurements

The stable chlorine isotope ratio ($^{37}\text{Cl}/^{35}\text{Cl}$) in perchlorate is normally analyzed by Isotope Ratio Mass Spectrometry (IRMS).^{10, 11, 41} However, we used Secondary Ion Mass Spectrometry (SIMS) for stable chlorine isotope ratio measurements because of the small sample size. All analyses were performed on TPAClO₄. Samples were mounted by pressing into indium metal in a 2.5-cm diameter sample holder and coating the surface with 50 nm of vapor-deposited gold. SIMS analyses were performed at the Center for Microanalysis of California Institute of Technology on an IMS 7f-GEO (CAMECA, Gennevilliers, France). Analyses were performed with a 10 keV Cs⁺ primary ion beam. The ion beam was focused to a diameter of ~20 μm with 5-6 nA of beam current. All isotope ratio analyses were performed by pre-sputtering of a 100 × 100 μm raster area for 120 sec, and then scanning a 75 × 75 μm raster during data collection. ³⁴SH contribution to ³⁵Cl results was negligible at a mass resolving power ($M/\Delta M$) of 1200 defined at the full width at 10% of the maximum peak height; this was also confirmed under a resolution of 5000. An energy bandwidth of 45 eV was set for all SIMS measurements, and secondary ion accelerating voltage was -9 keV for all isotopic analyses. Chlorine isotopes ³⁵Cl and ³⁷Cl were measured by Faraday cups with data collection times of 1 sec and 2 sec per cycle, respectively, for a total of 20 cycles. Data are normalized to measurements of KClO₄ isotopic reference materials USGS37 and USGS38,¹¹ which were converted to TPAClO₄ prior to measurement. Stable chlorine isotope ratios are reported in the conventional delta (δ) notation, as follows:

$$\delta^{37}\text{Cl} (\text{‰}) = \left[\left(\frac{^{37}\text{Cl}/^{35}\text{Cl}}{\text{sample}} \right) / \left(\frac{^{37}\text{Cl}/^{35}\text{Cl}}{\text{SMOC}} \right) - 1 \right] \times 1000$$

where SMOC is the isotopic reference Standard Mean Ocean Chloride.⁶⁰ Analytical precision corresponding to 1σ for δ³⁷Cl values determined from replicate measurements of reference materials is ±1.0 ‰.

AMS Measurements

After the analysis of the stable chlorine isotope ratios by SIMS, the remaining samples were scraped from the indium metal sample holders and diluted with USGS37 standard in TPAClO₄ form and homogenized by dissolving in 2 mL acetone. Sample J-1183 (Atlanta, USA) was diluted about 3.8 times, whereas sample J-1184 (Taltal, Chile) was diluted about 3.1 times, in order to get a larger sample size to facilitate loading of AgCl targets for AMS measurements. Then, the diluted perchlorate samples were converted from TPAClO₄ to KClO₄ by using 0.5 mol/L KOH in absolute ethanol solution, and the KClO₄ was sealed under vacuum into 20-cm lengths of 9-mm outer diameter borosilicate glass tubing. Afterwards, KClO₄ was heated for 30 minutes at 600°C in order to decompose KClO₄ according to the following reaction: $\text{KClO}_4 \Rightarrow \text{KCl} + 2 \text{O}_2(\text{g})$. Subsequently, KCl was converted into AgCl, which was used as a target material for the measurements of radioactive ³⁶Cl isotopic abundances by Accelerator Mass Spectrometry (AMS). Samples for the ³⁶Cl abundances were analyzed at the Purdue Rare Isotope Measurement (PRIME) Laboratory at Purdue University. The ³⁶Cl results were corrected for the instrumental

background and are reported in units of $^{36}\text{Cl}/\text{Cl} \times 10^{-15}$ along with errors based on counting statistics.

Comparative Isotopic Patterns

Chlorine-36 has previously been shown to be an effective tracer of the origin of perchlorate in various environmental matrices.⁴² Previous work indicates unique clustering of $^{36}\text{Cl}/\text{Cl}$ ratios vs. $\delta^{37}\text{Cl}$ values for perchlorate extracted from synthetic perchlorate, natural perchlorate from Atacama (Chile), and natural perchlorate from the southwestern USA.^{41, 42} The chlorine isotope pattern for synthetic perchlorate was defined based on analysis of laboratory grade perchlorate salts. The chlorine isotope pattern for natural perchlorate indigenous of the southwestern USA was extracted from groundwater and soil samples collected from Texas, New Mexico and California. The chlorine isotope pattern for natural perchlorate from the Atacama Desert was characterized based on bulk soil and groundwater samples collected in that region. Concentration ellipses were computed using the “data. Ellipse” function in the CAR (Companion to Applied Regression)⁶¹ package of R, an open source software environment for statistical computing and graphics,⁶² based on a bivariate normal distribution fit to the $^{36}\text{Cl}/\text{Cl}$ ratios and $\delta^{37}\text{Cl}$ variables of perchlorate reference materials. The concentration ellipses define the confidence curves within which 95% of the data is expected to lie, assuming a bivariate normality.

RESULTS AND DISCUSSION

The chlorine isotopic compositions of collected samples from the three known principal environmental sources of perchlorate in the United States and composite urine samples from Atlanta, USA and Taltal, Chile define three distinct, non-overlapping clusters in a diagram of $^{36}\text{Cl}/\text{Cl}$ as function of $\delta^{37}\text{Cl}$ (Figure 1). Natural perchlorate samples collected from the southwestern region have the highest values of $^{36}\text{Cl}/\text{Cl}$ ($3,100 \times 10^{-15}$ to $28,800 \times 10^{-15}$) and a range of $\delta^{37}\text{Cl}$ values from -3.7 to 4.5 ‰. The Atacama Desert samples have much lower values of $^{36}\text{Cl}/\text{Cl}$ ranging from 22×10^{-15} to 590×10^{-15} and $\delta^{37}\text{Cl}$ values of -14.3 to -11.8 ‰ than those of the southwestern region. Most of the synthetic perchlorate samples have $\delta^{37}\text{Cl}$ values in the range 0.2 to 1.6 ‰ and $^{36}\text{Cl}/\text{Cl}$ ratios of 0.0×10^{-15} to 40×10^{-15} which is consistent with a predominantly marine source of the brine used as a source of chloride ion.^{42, 63}

The urinary perchlorate sample from the Atlanta region more closely aligns with indigenous natural perchlorate extracted from groundwater and soil samples from the southwestern United States^{41, 42} in terms of its $\delta^{37}\text{Cl}$ value and $^{36}\text{Cl}/\text{Cl}$ ratio [$\delta^{37}\text{Cl} = +4.1 \pm 1.0$ ‰; $^{36}\text{Cl}/\text{Cl} = 1811 (\pm 136) \times 10^{-15}$] (Table 1) indicating indigenous natural perchlorate as the primary source of exposure in the sampled Atlanta residents (Figure 1). Any addition of synthetic or Atacama perchlorate would reduce the ^{36}Cl abundance, while also shifting the $\delta^{37}\text{Cl}$ result toward lower values on Figure 1 since both synthetic and Atacama perchlorate have lower $\delta^{37}\text{Cl}$ values than indigenous natural perchlorate from the United States. Overall, the shift in the $\delta^{37}\text{Cl}$ value appears to be minimal in the Atlanta sample relative to southwestern United States perchlorate, but the ^{36}Cl abundance is somewhat lower than common southwestern United States perchlorate, indicating negligible

Atacama perchlorate contribution since it would produce a much larger shift in the $\delta^{37}\text{Cl}$ value. However, a minor synthetic perchlorate contribution to a dominantly indigenous natural source could possibly explain both the $\delta^{37}\text{Cl}$ value and the $^{36}\text{Cl}/\text{Cl}$ ratio of the Atlanta urinary perchlorate sample.

Perchlorate $\delta^{37}\text{Cl}$ value and $^{36}\text{Cl}/\text{Cl}$ ratio [$\delta^{37}\text{Cl} = -11.0 \pm 1.0 \text{ ‰}$; $^{36}\text{Cl}/\text{Cl} = 254 (\pm 40) \times 10^{-15}$] determined from the urine of residents from Taltal, Chile (Atacama region) are similar to perchlorate samples collect from the Atacama region, indicating natural Atacama perchlorate to be the main source of exposure in that region (Figure 1). Perchlorate contributions from synthetic or young atmospherically produced perchlorate appear to be negligible, because any synthetic perchlorate contribution would increase the $\delta^{37}\text{Cl}$ value and decrease the ^{36}Cl abundance. Otherwise, addition of significant quantities of young atmospheric perchlorate would increase the ^{36}Cl abundance while preserving the $\delta^{37}\text{Cl}$ value if we assume that the chlorine sources for atmospheric perchlorate formation in a given region have relatively constant $\delta^{37}\text{Cl}$ value over time.

It was hypothesized that a few samples with anomalously high $^{36}\text{Cl}/\text{Cl}$ ratios in perchlorate from the southwestern US might have been affected by the presence of the bomb-produced ^{36}Cl pulse from the 1950s thermonuclear tests (Figure 1).⁴² However, $^{36}\text{Cl}/\text{Cl}$ ratios above $8,000 \times 10^{-15}$ were also measured in perchlorate extracted from southwest US groundwater having ^{14}C ages of more than 10 ka.⁴² The $^{36}\text{Cl}/\text{Cl}$ ratios of the indigenous natural perchlorate demonstrated that even the lowest $^{36}\text{Cl}/\text{Cl}$ value of about $3,100 \times 10^{-15}$ in perchlorate is much higher than the highest pre-bomb $^{36}\text{Cl}/\text{Cl}$ value of about $1,200 \times 10^{-15}$ in meteoric chloride near the Earth's surface.^{64, 65} Thus, the stratosphere is the only known location that has sufficiently high ^{36}Cl isotopic abundances⁶⁶ to account for the observed $^{36}\text{Cl}/\text{Cl}$ ratios in perchlorate samples from the southwestern US as well as in the urinary perchlorate sample from the Atlanta region, which strongly indicates a stratospheric origin for the indigenous natural perchlorate and the urinary perchlorate from Atlanta, USA.

The $^{36}\text{Cl}/\text{Cl}$ ratios in natural Atacama perchlorate samples are significantly lower compared to those in the indigenous natural perchlorate from the southwestern US, which might be explained chronologically since Atacama perchlorate is much older than the southwestern US perchlorate. Chilean nitrate deposits have an estimated three to eight million years (more than ten ^{36}Cl half-lives) of accumulation time^{67, 68} compared to the much shorter (on the order of tens of thousands of years) accumulation time for the indigenous natural perchlorate in the arid southwestern US. Thus the indigenous natural perchlorate would be expected to retain most of its initial ^{36}Cl signature.⁴¹ The low $^{36}\text{Cl}/\text{Cl}$ ratios in synthetic perchlorate are consistent with chloride sources from ancient marine halite deposits.⁴² Thus the ^{36}Cl signature along with the stable chlorine isotope of perchlorate is a valuable tool, which can be used for tracing the source and origin of perchlorates in the environment. Although not analyzed in this study, stable oxygen isotopes ($\delta^{18}\text{O}$, ^{17}O) of perchlorate offer additional tools for identifying perchlorate sources and origin.^{10-13, 41, 55, 69}

Our results demonstrate the use of chlorine isotope ratios of perchlorate extracted from urine for identifying the primary sources of perchlorate exposure in pooled human urines from two distinct locations. This appears to be a robust approach because the perchlorate

molecule is stable in the environment, as well as *in vivo*,³¹ and can apparently retain its initial isotopic composition for centuries to millennia in groundwater or surface water systems.^{56, 70} The isotopic identification of perchlorate exposure sources can aid in targeting efforts to reduce exposure and improve public health.

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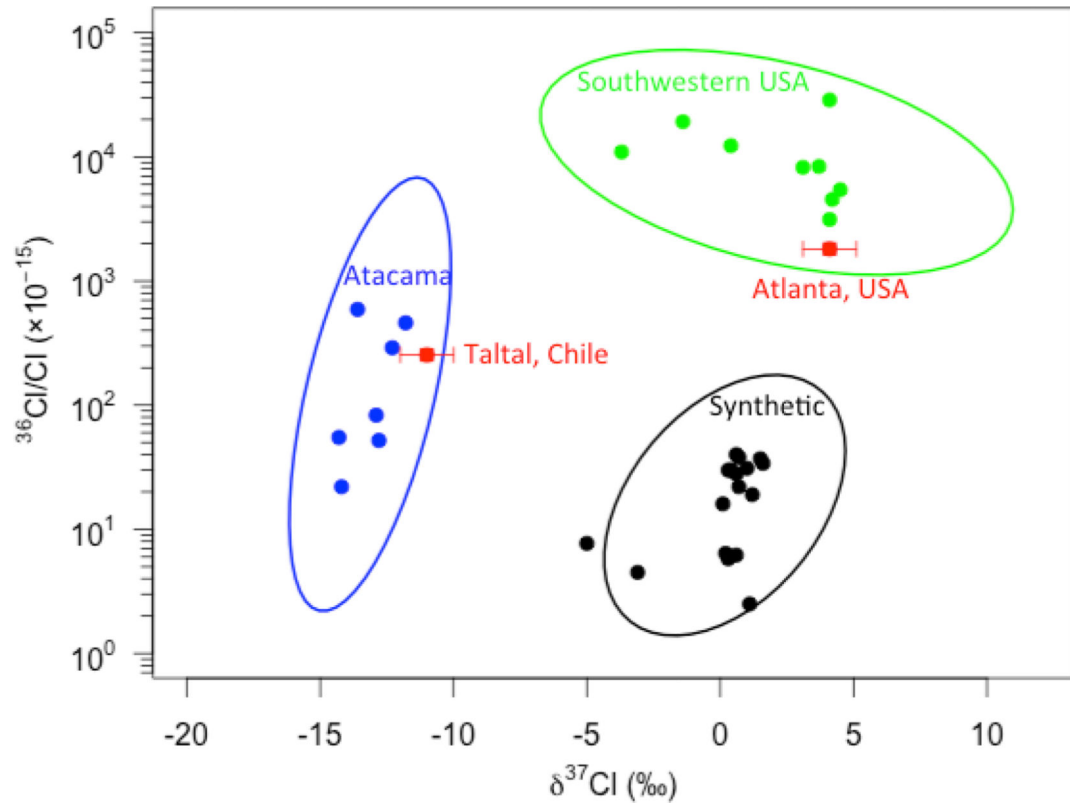


Figure 1.

Diagram comparing $^{36}\text{Cl}/\text{Cl}$ ratios vs. $\delta^{37}\text{Cl}$ values for perchlorate extracted from urine from residents of the Atlanta, USA metro area and Taltal, Chile (Atacama region), in comparison with synthetic perchlorate, and natural perchlorate from Atacama (Chile) and the southwestern USA.^{41, 42} $^{36}\text{Cl}/\text{Cl}$ errors are smaller than data points. The concentration ellipses define the confidence curves within which 95% of the data is expected to lie, assuming bivariate normality.

Table 1

Stable and radioactive chlorine isotope ratios of perchlorate extracted from urine from Atlanta, USA and Taltal, Chile regions.

| Sample ID | Sample Location | Urine Sample Volume (L) | ClO ₄ ⁻ on The Column (µg) | Final ClO ₄ ⁻ Recovered (µg) | δ ³⁷ Cl _{SMOC} (‰) | ³⁶ Cl/Cl (10 ⁻¹⁵) |
|---------------|-----------------|-------------------------|--|--|--|--|
| J-1183 | Atlanta, USA | 40 | 198 | 202 | +4.1 ± 1 | 1811±136 |
| J-1184 | Taltal, Chile | 1.05 | 154 | 155 | -11.0 ± 1 | 254±40 |

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