Arsenic -now part of a complete breakfast (for bacteria, that is)

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If there is one thing we can say for certain in science, it is that very rarely can anything be said for certain. It has long been held that all of life requires six essential elements known as bio-elements: carbon, oxygen, hydrogen, nitrogen, sulfur, and phosphorus. These elements compose all proteins, lipids, and nucleic acids, and their function is aided by select trace elements, typically metals or metalloids. With such a delicate and crucial formation of the building blocks of life, it would seem unlikely for there to be any room for deviation. Or so we thought. Scientists have found, however, that substitution of similar trace elements occurs in a variety of cellular components. Examples include interchanging copper for iron as a carrier of oxygen in some invertebrates and cadmium for zinc in certain enzymatic pathways.[1] A significant consideration of these substitutions is the analogous nature of the elements themselves. Each of the new molecules is similar to the molecule it is replacing in regard to chemical characteristics. Most of the eligible trace elements are in the same periodic group as the elements they exchange with, emphasizing their similarities in electronegativity, orbital configuration, and numbers of valence electrons

Understanding that substitution can occur with trace elements is paramount in hypothesizing about a synonymous switch in the major bio-elements. Substitution of bio-elements has never been observed–nor thought to be possible–but a knowledge of the intricacies that make possible the exchanges in trace elements paired with a fascinating discovery in California has forced scientists to reevaluate this notion. Dr. Felisa Wolfe-Simon's discovery of a bacterial strain in Mono Lake, California, may present the first known case of a living organism to exchange an analog for one of the six bio-elements; in this case, arsenic for phosphorus.[1]

Collections of detective novels and the alleged deaths of historical figures have sealed arsenic's fate as being known colloquially as a poison. Arsenic, sitting just below phosphorus on the periodic table, is a chemical analog of this crucial bio-element. The analogous nature of the parent element also transfers to other forms of the molecule; in this case, the relationship between phosphate (PO_4^{3-}) and arsenate (AsO_4^{3-}). Arsenate and phosphate are related closely enough that metabolic pathways in the body cannot distinguish between the two molecules. If arsenate is present in the body, it can be used in place of phosphate, creating major complications in the downstream steps of these pathways. These pathways involve the creation of nucleic acids and energy molecules like adenosine triphosphate (ATP), and thus require extremely stable molecules for their formation. Phosphate is chemically stable throughout these metabolic pathways and can therefore make up the backbone of nucleic acids. Arsenate is more easily hydrolyzed and has too short of a lifetime to form the molecules directed by the aforementioned cellular events. As a result, the analogous nature of arsenate and phosphate leads to the toxicity of arsenic, as metabolic pathways that mistakenly substitute arsenate for phosphate cannot produce a viable product. Since these pathways are absolutely crucial to cellular function, the results are fatal.[1]

The presence of phosphate in the bacterium, or lack thereof, became the focal point of the study done by Dr. Wolfe-Simon and her co-researchers. The bacterium GFAJ-1, a member of the family *Halomonadaceae*, was isolated from Mono Lake, a hypersaline lake with alkaline conditions and a relatively high concentration of dissolved arsenic. In order to perform tests in a laboratory setting that simulated the natural environment of this bacterium, the scientists used lake sediments as inocula into an artificial medium at pH 9.8 containing glucose, trace minerals, and vitamins. The medium contained increasing arsenate concentrations in a range of 100 μM-5mM, but had no added phosphate or phosphorus-containing compounds. Trace amounts of phosphate were present in the medium as a result of impurities in the other nutrients added, but these concentrations were exceedingly low. Upon transferring a colony into a liquid form of the medium from the agar, the team progressively increased the arsenate concentration to detect the optimal level for growth. They found the optimal concentration of arsenate to be 40 mM with no added phosphate. When phosphate was added, the bacteria grew considerably faster, indicating that the use of phosphate is still preferred over the relatively unstable arsenate. To verify that arsenate-dependent growth was indeed occurring in the samples without additional phosphate, a negative control was set up with no added arsenate. After incubation, Wolfe-Simon and her team did not observe any growth, signifying that the trace phosphate present in the media was not sufficient to support growth. Due to the fact that GFAJ-1 grew more extensively in the presence of added phosphate, the bacterium is not considered an obligate arsenophile, but showed arsenic-dependent growth. In short, GFAJ-1 can grow solely on arsenic without the use of phosphate, but also can incorporate phosphate into its metabolic processes when available.[1]

With evidence that GFAJ-1 actively uses arsenate for growth, the researchers extracted and gel-purified genomic DNA and positively identified arsenate in the sample. Experiments with radiolabeled arsenate confirmed the incorporation of arsenate into key biomolecules, and X-ray and other spectroscopic studies provided evidence that arsenate served a similar function as phosphate in DNA, composing the backbone. Although the study sheds significant light on the subject of major bio-elemental substitution, scientists are unclear about the mechanism by which arsenic is incorporated into the structure of biomolecules.[1]

Dr. Wolfe-Simon and her team have come under intense criticism since the publication of the paper in December of last year, including scathing blog posts by scientists in the field and harsh criticism by peers in other media outlets. Issues with the study stem from a wide spectrum of scientists, including microbiologists and astrobiologists. The competence of the team's methodologies remains a focal point of the scientific debate. Some researchers do not think that arsenic is incorporated into the structure of nucleic acids, citing shortcomings of analyzing gel-purified DNA or other sources of the observed arsenic. Dr. Rosie Redfield, a microbiologist at the University of British Columbia who issued an abrasive attack in her blog just days after the article was published, argues that an analysis of DNA embedded in a gel could potentially pick up arsenic present in the gel which is not structurally associated with DNA.[2] Dr. Barry Rosen of Florida International University is also hesitant to jump on the arsenic bandwagon, saying his primary concern is that arsenic is being packaged into the bacterium's vacuoles and not expressed in the nucleic acids.[3]

Another principle criticism of the study which has been cited by a number of individuals is the pace at which the results were published. A resounding concern from many in science is that the experiments and investigative procedure lacked thoroughness. Experts in the field have identified a number of tests they believe should have been performed before publication. In an interview with *Science*, Dr. Wolfe-Simon addresses these criticisms, explaining that the suggested tests were not performed due to a lack of available resources. When asked about the rapid nature of publishing, she clarifies that her team decided to publish as soon as possible because they lacked the proper tools to take the study to the next level, and that publishing would likely pique the interest of other labs with more resources who would be interested in collaborating on the project. By publishing the article when they did, the information was given to the scientific community with the hope of inspiring others to become involved with researching the topic further.[4]

Upon first glance, the criticisms at the forefront of this scientific debate seem harsh and, in some cases rather scathing; there has certainly been more criticism than praise. With closer examination, however, we realize that these discussions work to promulgate the focal points of science: discovery and debate. To this day, some of the most influential discoveries in science were presented to an audience whose reactions spanned the spectrum from delving further into the topic, to issuing biting criticisms of the methodologies, to blatantly calling the scientist a liar. In many of these cases, such findings were published in times when people feared changes in the norms that they had held for centuries, or where shaking the foundation of religion was considered unacceptable. Although Copernicus died before he became embroiled in controversy over his theory of heliocentrism, Galileo spent the remainder of his life under house arrest for defending his predecessor's work. Charles Darwin faced scrutiny for the rest of his life after publishing *On the Origin of Species*, and his theories have been continuously attacked through the present day. If anything, this goes to show the importance of scientific discovery and its ensuing debate, which can have vast consequences on science.

It is no mystery that additional research needs to be done on the topic, and with the buzz in the media and the scientific community, I would be surprised if researchers do not jump at the opportunity. Additional research using materials and methods unavailable to Dr. Wolfe-Simon and her team has the potential of making all the difference. Dr. Erica Suchman, professor of microbiology at Colorado State University, says she is excited to see additional research done to either confirm or dispel the notion that arsenic can be incorporated into nucleic acids. "It would be a huge paradigm shift for science. It would prove once again that bacteria perform some of the most extreme functions of all organisms."[5]

If there is anything else that can be said for certain in science, it is that scientific debate will forever be an essential constant. This is how science was designed to work, this is how science has worked for thousands of years, and this is how science will continue to work. The length and nature of the debate are intrinsically related to the magnitude of the discovery: major scientific discoveries have been accompanied by years–if not decades–of scientific debate. This should not deter scientists from publishing. Instead, we must realize that this is necessary for maintaining the credibility and upholding the integrity of science. Dr. Wolfe-Simon's discovery of a bacterium with the potential to substitute one of the major bio-elements should be afforded no pass on this criterion. Both Copernicus and Darwin recognized that their theories would draw largely negative reactions and they both delayed publishing for some time, fearful of the scientific community's response. They both understood, though, that their work could not be withheld from science and that scrutiny of their work would ultimately lead to a better scientific understanding, whether that entailed acceptance or rejection of their theories.

Scientists, intrinsically, do not respond well to changes in the foundation they have built their careers on. Even today, critics attempt to dismantle Darwin's ideas of evolution. His work, however, has withstood one hundred fifty years of such criticism and persists to this day. This is a result of thorough science and constructive debate. Now, the results of the GFAJ-1 experiment are subjected to the same test, the test of time. If further research confirms this microbial action and her findings are upheld, it may be regarded as one of the major discoveries in science.

References

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