NRC Publications Archive
Archives des publications du CNRC

Comment on “glyphosate and fluoride in high-hardness drinking water are positively associated with chronic kidney disease of unknown etiology (CKDu) in Sri Lanka”

Dharma-wardana, M. W. C.

This publication could be one of several versions: author’s original, accepted manuscript or the publisher’s version. / La version de cette publication peut être l’une des suivantes : la version prépublication de l’auteur, la version acceptée du manuscrit ou la version de l’éditeur.
For the publisher’s version, please access the DOI link below./ Pour consulter la version de l’éditeur, utilisez le lien DOI ci-dessous.

Publisher’s version / Version de l'éditeur:
https://doi.org/10.1021/acs.estlett.3c00879
Environmental Science & Technology Letters, 11, 3, pp. 288-289, 2024-02-28

NRC Publications Archive Record / Notice des Archives des publications du CNRC :
https://nrc-publications.canada.ca/eng/view/object/?id=179a15b3-4a2e-42f4-8323-6772e1da3883
https://publications-cnrc.canada.ca/fra/voir/objet/?id=179a15b3-4a2e-42f4-8323-6772e1da3883

Access and use of this website and the material on it are subject to the Terms and Conditions set forth at
https://nrc-publications.canada.ca/eng/copyright
READ THESE TERMS AND CONDITIONS CAREFULLY BEFORE USING THIS WEBSITE.

L’accès à ce site Web et l’utilisation de son contenu sont assujettis aux conditions présentées dans le site
https://publications-cnrc.canada.ca/fra/droits
LISEZ CES CONDITIONS ATTENTIVEMENT AVANT D’UTILISER CE SITE WEB.

Questions? Contact the NRC Publications Archive team at PublicationsArchive-ArchivesPublications@nrc-cnrc.gc.ca. If you wish to email the authors directly, please see the first page of the publication for their contact information.

Vous avez des questions? Nous pouvons vous aider. Pour communiquer directement avec un auteur, consultez la première page de la revue dans laquelle son article a été publié afin de trouver ses coordonnées. Si vous n’arrivez pas à les repérer, communiquez avec nous à PublicationsArchive-ArchivesPublications@nrc-cnrc.gc.ca.

National Research Council Canada
Conseil national de recherches Canada

Environmental Science & Technology Letters
pubs.acs.org/journal/estlcu
Correspondence

Comment on "Glyphosate and Fluoride in High-Hardness Drinking Water Are Positively Associated with Chronic Kidney Disease of Unknown Etiology (CKDu) in Sri Lanka"

Cite This: *Environ. Sci. Technol. Lett.* 2024, 11, 288−289

Read Online
ACCESS | Metrics & More | Article Recommendations

Ulrich et al.[1] claim a positive association among glyphosate (GLY), fluoride, high-hardness drinking water (HW), and chronic kidney disease of unknown etiology (CKDu). Invoking claims of glyphosate causing kidney damage and mitochondrial damage in zebrafish, they implicate glyphosate in the etiology of CKDu. In fact, we show below that their data taken as is provide strong evidence that glyphosate in any form is not implicated in the etiology of CKDu.

Ulrich et al.[1] report that fluoride (F^-), hard water, V, Sr, Rb, and GLY are strongly correlated with an odds ratio of >0.5, with glyphosate being nearly 3.5 times more associated with fluoride for endemic wells. Fluoride and glyphosate correlation is their main claim.

The data analysis uses concentrations expressed in grams per liter, etc., and not in moles per liter, thus ignoring differences in molecular and atomic weights (e.g., GLY, molecular weight of 169; Li, atomic weight of 6.9), producing nonphysical correlations that exaggerate GLY by a factor of ∼200.

Hard water (HW) is a mixture of hydrated Ca and Mg cations and anions such as CO_3, HCO_3, SO_4, and even PO_4. These need separate treatment if other alkaline earths (such as Sr and Rb) and fluoride are treated as independent variables, especially for the chemistry of regolith aquifers. Fluoride is the only anion treated in ref 1. We also include CO_3 for the sake of clarity. Humic (organic) and silicic acids, bases, and ion solvation are also ignored in ref 1. We denote them as X.

We treated HW explicitly as a standard mixture of Ca and Mg carbonates. Chemical associations are reported in ref 1 in the form $\{Ca_{i1}Mg_{i2}Sr_{i3}$, ..., etc.} for cations and $[F_{j1}(CO_3)_{j2}...]$ for anions, using molar concentrations. GLY and other chemical moieties of interest are written as $|GLY_{k1}X_{k2}...|$.

Using the average molar concentrations based on the 75th percentile given in Tables S3−S6 of the Supporting Information of ref 1, we rewrite ionic-association formulas as follows. The number of fluoride ions is normalized to unity for non-endemic wells.

non-endemic wells $\{Ca_{4.5}Mg_{3.2}Sr_{0.061}Rb_{0.004}...\}$

$[(CO3)_{8.6}\mathbf{F_1}...]|GLY_{0.00009}X...|$

eddemic wells

$\{Ca_{16.3}Mg_{9.5}Sr_{0.231}Rb_{0.0006}...\}[(CO3)_{25}\mathbf{F_{2.7}}...]|GLY_{0.00032}X...|$

This "molecular" representation of the Ulrich data[1] shows that while there are nine glyphosate moieties per 10 000 fluoride ions in non-endemic well water, there are <12 GLY moieties in endemic wells. Therefore, the difference in the probability of a fluoride ion encountering a glyphosate molecule in an endemic well, as compared to a non-endemic well, is a mere 0.03%. Furthermore, some non-endemic wells with 2.97 μg/L show more glyphosate per fluoride ion. Therefore, the "increased" correlation with fluoride in CKDu-endemic wells has no significance, being within well-to-well random fluctuations.

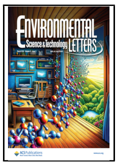
The difference between endemic and non-endemic wells becomes even smaller if the Ca−glyphosate chelate (molecular weight of 209) is used as the relevant chemical moiety. Rates of chemical reactions as well as toxicokinetic rate processes are proportional to the concentrations of the reacting species or to some power thereof. By this analysis, there is no difference in toxicity significance in non-endemic wells and endemic wells.

The Gibbs free energy of a cluster of ions, inclusive of solvation effects, can indicate ion clustering. Such calculations revealed[2] that fluoride and magnesium ions may persist as $(MgF)^+$-type transients. The synergy of such complexes on CKDu was established by Wasana et al.[3]. Similar calculations with the GLY component, even at higher concentrations than in CKDu-endemic wells, show no stabilization because the chelation generates very low ambient concentrations of GLY. In effect, hard water protects against any possible glyphosate toxicity but enhances fluoride toxicity.

CKDu may arise from cumulative effects of environmental agents whose nature is mired in controversy.[4] Fluoride and possibly magnesium ions present together have been favored in several studies.[5] In the assessment with pesticide effects, a time average taken over at least two planting seasons is necessary. Correlations, when found in a single-shot study while marred by some control wells being in noncomparable climate zones, e.g., at Matara compared to Padaviya, are not meaningful because multiple time measurements are needed.

According to Ulrich et al.,[1] "Glyphosate can tightly chelate divalent metal cations ... These glyphosate−metal complexes increase the half-life of the herbicide dramatically, from 90 days

Received: December 4, 2023
Revised: December 21, 2023
Accepted: February 23, 2024
Published: February 28, 2024



to 7 years in water and from 47 days to 22 years in soil. This behavior makes glyphosate a potential contributor to CKDu".

Such long persistence established for cold climates is sharply reduced to a few days for the Sri Lankan dry zone where the average temperature *T* that is present in the Arrhenius factor in the decay rate exceeds 30 °C. The tightly chelated glyphosate—metal complex is NOT glyphosate and not a herbicide but a strongly inert insoluble substance. The presence of some algae and aquatic weeds in these wells shows that there is no active herbicide in the water. The dose used is said to be "metal concentrations ... found in CKDu endemic reservoirs and wells". If the latter is a threshold for humans (average weight of 60 kg), then the dose used for zebrafish (average wright of 150 mg) is some 400 000 times the human threshold.

What has been studied with zebrafish is acute toxicity and has no relevance to chronic toxicity.

M. W. C. Dharma-wardana orcid.org/0000-0001-8987-9071

AUTHOR INFORMATION

Complete contact information is available at:
https://pubs.acs.org/10.1021/acs.estlett.3c00879

Funding

Open access funded by the National Research Council Canada Library

Notes

The author declares no competing financial interest.

REFERENCES

(1) Ulrich, J. C.; Hoffman, K.; Gunasekara, T. D. K. S. C.; Sandamini, P. M. M. A.; Jackson, B. P.; De Silva, P. M. C. S.; Jayasundara, N.; Ferguson, P. L. Glyphosate and Fluoride in High-Hardness Drinking Water Are Positively Associated with Chronic Kidney Disease of Unknown Etiology (CKDu) in Sri Lanka. *Environ. Sci. Technol. Lett.* **2023**, *10* (10), 916−923.

(2) Dharma-wardana, M. W. C. Chronic kidney disease of unknown etiology and the effect of multiple-ion interactions. *Environ. Geochem Health* **2018**, *40*, 705−719.

(3) Wasana, H. M. S.; Perera, G. D. R. K.; Gunawardena, P. D. S.; Fernando, P. S.; Bandara, J.; et al. WHO water quality standards vs synergic effect(s) of fluoride, heavy metals and hardness in drinking water on kidney tissues. *Sci. Rep.* **2017**, *7*, 42516.

(4) Balasooriya, S.; Munasinghe, H.; Herath, A. T.; Diyabalanage, S.; Ileperuma, O. A.; Manthrithilake, H.; Daniel, C.; Amann, K.; Zwiener, C.; Barth, J. A. C.; Chandrajith, R. Possible links between groundwater geochemistry and chronic kidney disease of unknown etiology (CKDu): an investigation from the Ginnoruwa region in Sri Lanka. *Exposure Health* **2020**, *12*, 823.

(5) Dharma-wardana, M. W. C. Chronic Kidney Disease of Unknown Etiology (CKDu) — The Search for Causes and the Impact of Its Politicization. In *Medical Geology, En route to One Health*; Prasad, M. N. V., Vithanage, M., Eds.; Wiley, 2023; Chapter 7.