

Project Title:

Elucidation of selective chemical binding on cations

Name:

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Description of the project

1. Background and purpose of the project, relationship of the project with other projects

Establishing efficient and transgenic-free phytoremediation system for radioactive cesium in eastern Japan, we adopted chemical biology approaches. A chemical library composed of 10,000 synthetic organic compounds was screened for chemicals which promote cesium accumulation in *Arabidopsis thaliana*. Fourteen chemicals were isolated as cesium accumulators and of those, one was characterised as a cysteine derivative, methyl cysteinate. Cysteine was also found to improve cesium accumulation in plants and internal cysteine concentrations were increased upon cesium treatment. By contrast, other cysteine derivatives and amino acids on the cysteine biosynthesis pathway did not show the cesium accumulation effect. It has been suggested that methyl cysteinate and cysteine bind to cesium either on the surface of roots or inside the plant cells and contribute to cesium accumulation in plants. To investigate the detailed mechanisms of Cs^+ transport and response in plants, we performed quantum mechanical calculation of binding strength of Cs^+ -cysteine complex and its derivatives.

2. Specific usage status of the system and calculation method

To evaluate the effective Cs^+ binding strength of the cysteine, thorough quantum mechanical

system of the ion-cysteine complex in aqueous systems have been constructed. Each system contains a chemical with 20 – 70 atoms including alkali metals, Na^+ , K^+ , Rb^+ and Cs^+ , to observe binding strength difference among the elements. All quantum calculations are calculated by the commercial software, Gaussian 09 which already had been installed on the supercomputing system. At first, we optimized chemical structures using density functional theory (DFT) approach with B3LYP hybrid exchange-correlation energy functional and the atom-centered LanL2DZ basis set for heavy ions, such as Rb^+ and Cs^+ . We assumed that the experimental condition is much more likely in water rather than vacuum. Therefore, to mimic the aqueous systems, the Polarizable Continuum Model (PCM) with the integral equation formalism variant have been used. After the chemical only optimization process, electrostatic potential (ECP) maps calculated to find more probable ion binding site. Figure 1 shows the ECP maps of one of candidate chemicals.

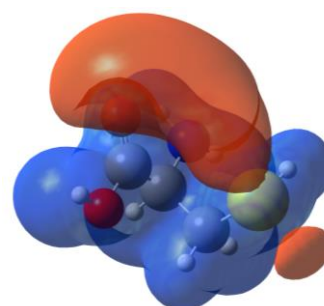


Figure 1. Solution phase electrostatic potential maps of cysteine.

As shown in Figure 1, in the solution phase, electrons are delocalized by surrounding water molecule. Thus, we could select more negative positions (in red) which an ion can bind to. After finding the ion bind positions, we placed four different ions, Na⁺, K⁺, Rb⁺ and Cs⁺, near the site.

Again, we optimized ion bind structures of each candidate chemicals in solution phase and obtained energy of ion binding structures.

After the calculation, we could evaluate the ion binding energy by using Eq. 1.

$$E_{binding} = E_{complex} - (E_{chemical} + E_{ion}) \quad (\text{Eq. 1})$$

Eventually, we could calculate the ion binding energy of cysteine and cysteine and its derivatives.

3. Result

In order to understand the Cs-cysteine bindings, quantum mechanical calculations were performed. In Figure 2 and 3, three possible cases of cesium binding were predicted for each chemical: Case 1 representing single interaction with the amino group, Case 2 representing chelating with the amino and sulfhydryl groups, and Case 3 representing chelating with the amino, sulfhydryl and ketone groups.

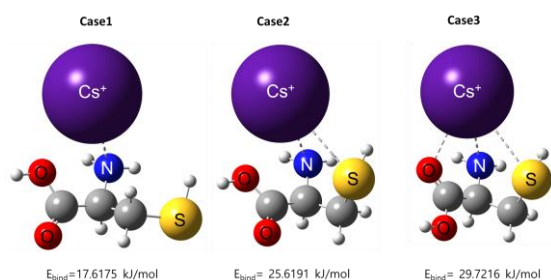


Figure 2. Three different Cs-cysteine binding forms.

Figure 4 shows methyl cysteinate and cysteine were predicted to have high enough maximum binding energy with cesium ion, 30.5 kJ mol⁻¹ for methyl cysteinate and 29.7 kJ mol⁻¹ for cysteine. A little lower binding energy in each case for cysteine relative to methyl cysteinate might explain the difference in the range of working concentrations for cesium accumulation. In addition, difference in dipole moments for methyl cysteinate and cysteine, 1.34 D and 1.14 D, respectively, may contribute to the stability of each cesium complex.

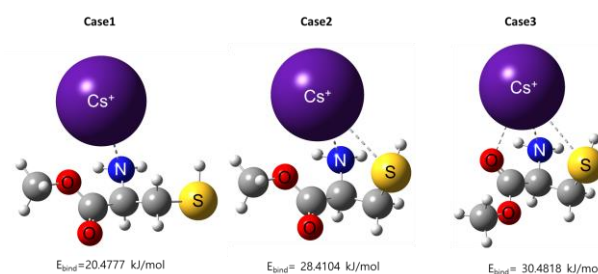


Figure 3. Three different Cs-Methyl cysteinate binding forms.

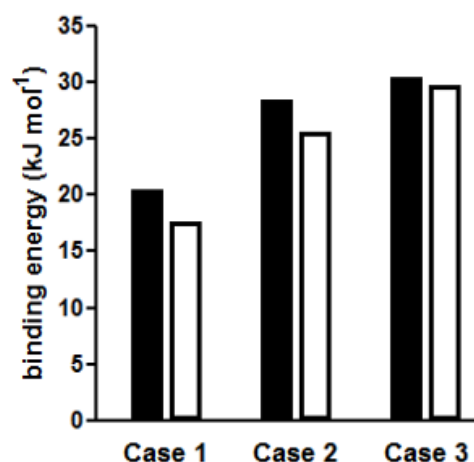


Figure 4. Binding energy of methyl cysteinate (black bars) and cysteine (white bars) with cesium for each case.

4. Conclusion

We have performed quantum mechanical calculation of Cs⁺ binding energies for cysteine and cysteine derivatives and obtained optimized structures, ECP maps and Cs⁺

binding energies of each chemicals. The results show the candidate chemicals have different Cs^+ binding properties in different ionic solution. However, all of them shows relatively high Cs^+ binding strength compare to other supramolecular interactions such as hydrogen bonding. Thus, we could assume that the candidate chemicals help Cs^+ uptake of plants. In the case of the zinc-cysteine complex, the sulfhydryl and amino groups of cysteine have been suggested as the actual binding sites, which corresponds with the high binding energy for Case 2 of methyl cysteinate and cysteine with cesium predicted from our calculations in Figure 2 and 3. (Li and Manning, 1955) The authors have also indicated that for the zinc and lead complexes, methyl cysteinate is less stable compared to cysteine, in contrast to what we observed for the case of cesium possibly due to the difference in ionic size. Methyl cysteinate was more effective in cesium accumulation and worked at the one order of magnitude lower concentrations compared to cysteine. This might be explained by higher dipole moment and higher binding energy with cesium for methyl cysteinate.

5. Schedule and prospect for the future

For the further study, we try to calculate the binding free energy of the complex using free energy perturbation method. After summarizing the computational and experimental results, we expect that the detail Cs^+ uptake mechanism can be revealed. Also, we are going to use effective method to find optimal ion binding position and get more precise ionic binding strength.

Usage Report for Fiscal Year 2016

Fiscal Year 2016 List of Publications Resulting from the Use of the supercomputer

[Publication]

1. Eri Adams, Takae Miyazaki, Aya Hayaishi-Satoh, Minwoo Han, Miyako Kusano, Himanshu Khandelia, Kazuki Saito, Ryoung Shin*. A novel role for methyl cysteinylglycine, a cysteine derivative, in cesium accumulation in *Arabidopsis thaliana*. **Sci. Rep.** 7, 43170; doi: 10.1038/srep43170 (2017)

[Oral presentation at an international symposium]

1. Ryoung Shin. Finding chemical compounds to enhance cesium tolerance or accumulation in plants. **The International Conference on Arabidopsis Research**. June 30, 2016, GyeongJu, Korea.