Polyoxometalates (POMs) are a group of metal-based oxygen clusters. Due to their diverse structural properties, solubility, redox potential and charge density, POMs have a wide range of applications in various fields such as heterogeneous catalysis, material science and medicine. Due to their large size, three-dimensional shape and high negative charge, POMs tend to specifically interact with proteins via electrostatic and hydrogen bonding interactions.[1] The affinity of POMs towards specific protein surfaces has been recently exploited to create a novel class of artificial enzymes for protein hydrolysis. By imbedding a strongly Lewis acid metal ion such as Zr(IV) and Ce(IV) into lacunary POMs, selective hydrolysis of a range of different proteins has been achieved. Kinetic studies have shown that Zr(IV) substituted POMs of Keggin, Wells-Dawson and Lindquist type are all active catalysts for the hydrolysis of Human Serum Albumin (HSA), insulin chain B and Horse Heart Myoglobin (HHM), however their efficiency depended on the type of POM structure into which the Zr(IV) ion was imbedded. Interestingly, recent examples have shown that the type of imbedded metal ion influences selectivity of hydrolysis.[2]

Recently, we reported the first co-crystal structure of a non-covalent complex formed between catalytically active 1:1 Zr(IV)-substituted Keggin POM, and Hen Egg White Lysozyme (HEWL).[3] Although the dimeric 1:2 Zr(IV)-substituted Keggin POM was used, the POM co-crystallized as the 1:1 species, giving the first crystallographic evidence for the existence of the monomeric Keggin species previously proposed to exist in solutions with very low pH by NMR spectroscopy. Here we present the complex between HEWL and the catalytically active 1:1 Hf(IV)-substituted Wells-Dawson POM. Again, the monomeric 1:1 form is present whereas the 1:2 complex was added to the crystallization mixture. The binding mechanism and position of this POM is similar to the previous structure. However, we observed binding of the POM with the Lewis acid metal directed towards the protein near a cleavage site, thus further supporting our hypothesis. These models will further guide the development of POMs as artificial proteases.


Keywords: polyoxometalate, artificial enzymes, protein hydrolysis