Renal Osmolyte Induced Perturbation to Hydrogen Bonding Structure of Water

P. K. Verma[1,2*] and M. Cho[1,2]

[1]Center for Molecular Spectroscopy and Dynamics, Institute for Basic Science (IBS), Korea University, Seoul 02841, South Korea

[2]Department of Chemistry, Korea University, Seoul 02481, South Korea

Osmolytes are an integral part of living organism, e.g., the mammalian kidney uses sorbitol, trimethylglycine, taurine and myo-inositol to counter the deleterious effects of urea and salt. The mode of operation of osmolytes has long been a controversial issue. One school of thought is direct interactions of osmolytes with protein backbone [1]. While the other believes indirect action where osmolytes modify solvent water's properties which in turn dictate the protein's stability in high osmolyte solutions [2]. Since the observables like solvation behavior obtained from thermodynamic measurement of protein-free binary solution of osmolytes correlates very well with their action on protein, we have focused on all the renal osmolyte solutions over wide concentration ranges [3].

Our findings confirm that the renal osmolytes (sorbitol, trimethylglycine, taurine and myo-inositol) do modulate the hydrogen bonding network and dynamics while the denaturant (urea) does not. This has been possible by employing two different vibrational probes, i.e., OD and azide stretch modes, that not only complement each other but also directly or indirectly participate in water H-bonding networks in high osmolyte solutions. The microscopic picture obtained from both experiments and MD simulations provides clear evidence that denaturant would perturb protein structure via direct interactions with protein itself, while the protecting osmolytes do indirectly through modulating water H-bonding structure even though the magnitude and spatial extent vary depending on the osmolytes. Apart from being of physicochemical and biochemical importance, these osmolytes are of biotechnological importance since they are energy-boosting ingredients or pharmaceutical excipients. We thus anticipate that studying the properties of such highly concentrated osmolyte solutions can shed light on properties of water inside living organism.

References:

[1] M. Auton, D. W. Bolen, and J. Rösgen, Proteins: Struct Funct Bioinform **73,** 802 (2008)

[2] C. J. Roche, F. Guo, and J. M. Friedman, J Biol Chem **281,** 38757 (2006)

[3] J. Rösgen, B. M. Pettitt, and D. W. Bolen, Biochemistry **43,** 14472 (2004)