

Protein stability and the Hofmeister series: the anion's increase of the solution surface tension enhances protein stability.

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We have investigated how the changes in the solution surface tension produced by the anions of the Hofmeister series affect protein stability, using the IGg binding domain of the protein L from *Streptococcal magnus* (ProtL) as a case study. To that end, a suite of lysine per glutamine modifications have been obtained and structurally and thermodynamically characterized. The changes in stability introduced with the mutation are related to the solvent accessible area of the side chain and ultimately produced by the solvation of the non-polar moiety of the residue. The thermostability for the set of ProtL mutants have been determined in the presence of varying concentrations (0-1M) of eight different sodium salts representative for the Hofmeister series of anions: sulfate, phosphate, fluoride, acetate, chloride, nitrate, perchlorate and thiocyanate. Upon cosolute addition, the stability changes produced by the anions are proportional to the surface changes introduced with the mutation and correlate with the increment in the solution surface tension introduced by the anion. Our results are consistent with a model where the raise in the solution surface tension induced by the anion stabilizes the folded conformation of the protein. This contribution shall be complementary to the non-specific and weak interactions between the ions and the protein backbone that shifts the equilibrium towards the unfolded state.