

Solvation and self-assembly of nucleic acids in non-conventional solvents/water mixtures: from the improved structural stability to the formation of ionogels

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Although nucleic acids are considered to be reasonably stable in aqueous solutions, there are several bottlenecks of DNA technology in water as a conventional bulk solvent. Since DNA in aqueous solutions is susceptible to oxidative and hydrolytic denaturation for long-term storage and its helix structure can be damaged by extreme conditions of temperature, pH and ionic strength, finding appropriate media that ensure the long-lasting stability of DNA and help to overcome the limitations of aqueous buffers remains a challenging task. This is a critical point especially for the molecular analysis of DNA in forensic science and biology where it is essential to optimize the storage of the sample to avoid loss of DNA quality. Moreover, this vulnerability limits the use of nucleic acids as building blocks for realizing innovative devices based on 3D ordered structures of DNA and hybrid materials in nanotechnology and biomedical technology. Using nucleic acids in non-conventional solvents such as ionic liquids (ILs) and deep eutectic solvents (DESs) offers a promising alternative to organic solvents both for stabilizing and preserving the native structure of DNA in solution over the long term and for designing innovative DNA nano-systems such as thermo-reversible ionogels with an unprecedented degree of freedom. This is thanks to the unique capacity of both these molecular liquids in acting as electrolytes and solvents. Additionally, when ILs and DESs are mixed with water, the resulting mixtures exhibit some interesting and unique properties that make them capable of behaving as functional fluids in DNA science [1-4]. In this contribution, we will address the question of the effectiveness of ILs versus DESs, in mixture with water, for the solvation and self-assembly of oligonucleotides and large nucleic acids. Even these molecular liquids are claimed to have similar physicochemical properties, recent studies evidenced that ILs and DESs exhibit substantial differences in the solvation behavior of bio-macromolecules such as DNA. The joint combination of advanced spectroscopic techniques such as synchrotron radiation-UV Resonance Raman spectroscopy (SR-UVR) and molecular dynamics (MD) simulations enables the measurement of experimental quantities directly related to pair hydrogen bond strength and base stacking forces in nucleic acid strands and the probing of structure specific interactions between the solvent and different sites of DNA. This approach allows to detect defined structural transitions of DNA that involve specific base-tracts during thermal unfolding pathway and to give a comprehensive description of the self-assembly mechanism leading to the formation of nucleic acid hydrogels. Overall these experimental-computational studies reveal a more effective thermal-protective effect operated by hydrated choline-based DESs on the double-helix structure of DNA respect to imidazolium-based ILs. This finding has been related to the establishment of preferential H-bonds interactions between specific DES moieties and the guanine and adenine bases in the DNA groove

that lead to a more effective stacking between of these bases even at high temperature values. These results could facilitate the designing of effective stabilizing eco-friendly organic co-solvents for their exploitation in biomedical and life science field.

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