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Study of the interaction of neurotoxic N-Methyl-4-(4’-hydroxyphenyl) pyridinium iodide with bovine serum albumin

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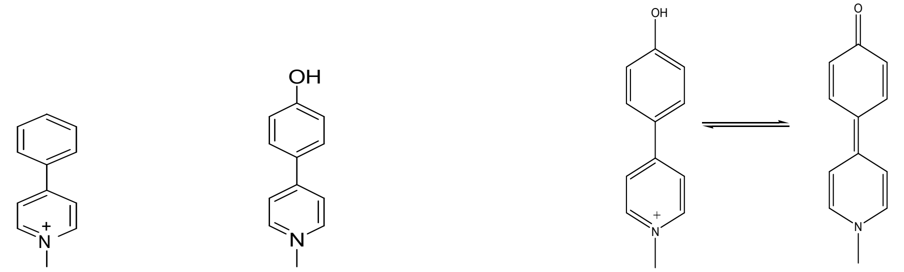
N-Methyl phenyl pyridinium salt (MPP^+) and its derivatives are known for its ability to bind to membrane bound protein complexes such as vesicular monoamine transporter (VMAT) and dopamine transporter (DAT) as well as enzymes such as cytochrome P_{450} and monoamine oxidase (MAO) B. Among these derivatives, 1-Methyl-4-(4’-hydroxyphenyl)pyridinium Iodide ($4OHMPP^+$ Scheme 1) has remarkable polarity dependent excited state properties and can be used as an excellent model to study the microenvironment of the “active site” of multiprotein complexes such as VMAT .



1 2 3a 3b

Scheme 1: N-Methyl phenyl pyridinium salt (MPP^+) and 1-Methyl-4-(4’-hydroxyphenyl)pyridinium Iodide ($4OHMPP^+$). 3a and 3b are the structural variation of **2** at different pH values, 5.50 and 7.45 respectively.

In this work, bovine serum albumin (BSA) is selected as our model to understand the interaction of $4OHMPP^+$ with protein because its wide range of physiological functions involving binding, transport and delivery of various biomolecules. The interaction of $4OHMPP^+$ and BSA was studied in aqueous buffer solution at pHs (5.50, 7.45) by fluorescence and UV-visible spectroscopy at 298K, 303K and 308 K. The binding mode, the binding constant and protein structure changes have been evaluated. The quenching constants K_q , K_{sv} and the association constant K were calculated by using Stern-Volmer equation based on the quenching of the fluorescence of BSA. It has been manifested that both dynamic and static quenching occurs between the quencher and the fluorophore and quenching data fit into the modified Stern-Volmer equation.

$$K_{APP} = \left(\frac{I_0}{I} - 1 \right) \frac{1}{[Q]} = (K_{SV} + K_S) + K_{SV} K_S [Q]$$

The thermodynamic parameters, the enthalpy (*ΔH*) and the entropy change (*ΔS)* were estimated by using van't Hoff equation. Quenching spectra of the BSA shows a red shift which indicates the changes of secondary structure of the protein upon binding of quencher.

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