Title of thesis: Optical Spectroscopic Studies on the Interaction of Prototropic Antibacterial Drugs and Photoacid with Biomacromolecular Hosts and Molecular Assemblies

Abstract

Host biomacromolecules, macrocycles, and molecular assemblies can control the photophysical and photochemical processes of guest fluorescent molecular probes in various ways. Pyranine is a fluorescent photoacid that is known to undergo the photochemical process, proton transfer in its electronic excited state. The intrinsic ligand binding characteristic of the biomacromolecular hosts like a protein can control the acid-base equilibrium of a prototropic guest ligand in very specific manner. In this thesis, I have explored the Excites state proton transfer (ESPT) process of the photoacid HPTS in a host protein lysozyme and in some molecular assemblies of neat and mixed ionic micelles. The protein lysozyme was found to modulate the acid-base equilibrium and the rate of proton transfer in the excited state of the photoacid in a distinctive manner. Addition of an *inert* electrolyte remodulated the proton transfer behavior of the protein-associated photoacid in the reverse manner. I have studied the ESPT nature of the photoacid by confining it into a neat pluronic micelle F127, ionic mixed micellar aggregates of F127-SDS and F127-CTAC systems; and also in neat TX100 micelle, ionic mixed micellear aggregates of TX100-SDS and TX100-CTAC systems. These mixed micelles of ionic surfactants with F127 or TX100 were detected to govern the ESPT behavior of the probe in quite diverse fashion dictated by the water accessibility around the location of the probe inside the host confinements.

A drug gets distributed in the target receptor site and also to other extra or intra cellular nonreceptor sites throughout the body after administration. Interaction of a drug-biomacromolecule pair can alter the conformation, activity of the concerned biomacromolecular host; and it can influence the pharmacokinetics of the drug in many ways. For a drug exhibiting pH dependent different protonation states, the pK_a of such drugs is an important factor relating to the drug pharmacokinetics. Now, the binding selectivity of the biomacromolecules towards the protomeric forms of a drug can perturb the equilibrium connecting the different protropic species of the drug, thus consequently influencing the pK_a related drug distribution. In this thesis, I have examined the interaction of an antibacterial

fluoroquinolone drug norfloxacin with the antimicrobial enzyme lysozyme; and interaction of few structurally different fluoroquinolone drugs with double stranded calf thymus DNA. The protein lysozyme was found to prefer one specific protomeric species, zwitterionic form of norfloxacin, guided by the specific interaction forces, molecular structure and ionic nature of the particular protomer and also pH of the medium. The preferential binding led to switchover from one protomeric species to the most favoured one. I have found in the study that the fluoroquinolone drugs interact with DNA in their protonation state dependent diverse manner. Some binding features were found to be dependent on the structure of the drugs, whereas some binding features were detected to be general irrespective to their molecular structure. Additionally drug displacement from the DNA bound state has been achieved by an external anionic micellar system.

Thus it has been found from the attempted studies that the excited state deprotonation dynamics and ground/excited state acid-base equilibria of photoacid and prototropic drugs undergo modulation in some specific manner depending on the interaction signature of protomeric forms with different hosts.