CHAPTER 4

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AIM AND OBJECTIVES

It is evident from the discussion in previous chapters that the binding of a drug to plasma protein reduces its free fraction in serum, thus reducing its availability for active uptake or diffusion into surrounding tissues and also significantly influencing its pharmacokinetics, toxicity, and etc\textsuperscript{1}. Besides these, as a criterion in pharmacokinetic parameters, pre-clinical and clinical studies, and the degree of binding of a compound to plasma proteins can provide important indications about the compound’s efficacy and its potential for drug-drug interactions\textsuperscript{2-4}. So, therefore, the determination of the amount of drug binding to plasma proteins is an essential step in both the discovery and clinical phases of drug development.

When a small molecule binds to plasma protein, the interaction is typically the result of strong ionic and hydrophobic interactions. Since blood contains hundreds of proteins, there is a high probability that most small molecules will exhibit some level of binding, and hence the importance of the study for understanding the mechanism of drug protein interaction and to have an insight into the aspects of drug availability in systemic circulation and drug discovery process.

This project work is undertaken to investigate the plasma protein binding aspects of the drugs selected namely nimesulide, diclofenac sodium, lamotrigine, and lamivudine. In some cases, the data regarding percent protein bound, stability constants and number of binding sites for plasma-protein binding of the above-mentioned drugs are available in the literature. But a thorough study regarding the probable mechanism of interaction and effects of some physico-chemical factors like pH, ionic strength and dielectric constant on protein binding of those selected drugs were missing. So our prime aim was to investigate in detail the binding of the above-mentioned drugs and to establish a probable
mechanism of drug protein interaction through thermodynamic approach. A detail study regarding the effect of pH, ionic strength, and dielectric constant of the dialyzing solvent on the stability constants of the drug-protein interaction processes were undertaken. The influence of species variation on plasma-protein binding of drugs was also studied.
REFERENCES: