studies. Circular dichroism (CD) is a fast and relatively easy spectroscopic technique to study protein conformational behavior. In this review examples of the applications of CD and synchrotron radiation CD (SRCD) to membrane protein ligand binding interaction studies are discussed. The availability of SRCD has been an important advancement in recent progress, most particularly because it can be used to extend the spectral region in the far-UV region (important for increasing the accuracy of secondary structure estimations) and for working with membrane proteins available in only small quantities for which SRCD has facilitated molecular recognition studies. Such studies have been accomplished by probing in the near-UV region the local tertiary structure of aromatic amino acid residues upon addition of chiral or nonchiral ligands using long pathlength cells of small volume capacity. In particular, this review describes the most recent use of the technique in the following areas: to obtain quantitative data on ligand binding (exemplified by the FsrC membrane sensor kinase receptor); to distinguish between functionally similar drugs that exhibit different mechanisms of action towards membrane proteins (exemplified by secretory phospholipase A2); and to identify suitable detergent conditions to observe membrane protein–ligand interactions using stabilized proteins (exemplified by the antiseptic transporter SugE). Finally, the importance of characterizing in solution the conformational behavior and ligand binding properties of proteins in both far- and near-UV regions is discussed. This article is part of a Special Issue entitled: Structural and biophysical characterization of membrane protein–ligand binding.

Xiao, Z. and A. G. Wedd (2010). "The challenges of determining metal-protein affinities." *Nat Prod Rep* 27(5):768–789.

A key property of metalloproteins and -enzymes is the affinity of metal ion M for protein ligand P as defined by the dissociation constant KD = [M][P]/[MP]. Its accurate determination is essential for a quantitative understanding of metal selection and speciation. However, the surfaces of proteins are defined by the sidechains of amino acids and so abound in good metal ligands (e.g., imidazole of histidine, thiol of cysteine, carboxylate of aspartic and glutamic acids, etc.). Consequently, adventitious binding of metal ions to protein surfaces is common with KD values > or = 10(−6) M. On the other hand, transport proteins responsible for 'chaperoning' essential metals to their cellular destinations appear to bind the metal ions selectively (KD < 10(−7) M, both for speciation and to minimize the toxic effects of 'free' metal ions. These ions are normally bound with still higher affinities at their ultimate destinations (the active sites of metalloproteins and -enzymes). This review surveys possible approaches to estimation of these dissociation constants and pinpoints the various problems associated with each approach.

Solubility

Allen, L. V., Jr. (2008). "Dosage form design and development." *Clin Ther* 30(11):2102–2111.

BACKGROUND: Drugs must be properly formulated for administration to patients, regardless of age. Pediatric patients provide some additional challenges to the formulator in terms of compliance and therapeutic efficacy. Due to the lack of sufficient drug products for the pediatric population, the pharmaceutical industry and compounding pharmacies must develop and provide appropriate medications designed for children. OBJECTIVE: The purpose of this article was to review the physical,