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Review

Binding of serum albumins with bioactive substances – Nanoparticles to drugs

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ABSTRACT

The interactions of human and bovine serum albumins (HSA and BSA) with various drugs and nanomaterials receive great attention in the recent years owing to their significant impact in the biomedical field. Although there are various techniques available for studying such interactions, fluorescence spectroscopy is the most appealing one due to its high sensitivity and straightforwardness. Detailed information about the interactions of drugs and nanomaterials with serum can be deducted from a mass of information accumulated by the fluorescence quenching studies. The present review emphasizes the interaction of various nanomaterials, antibiotics, anticancer drugs, anti-inflammatory agents, dyes, flavonoids, and certain noxious materials with HSA and BSA. In particular, we focus on the interactions of serum albumin with nanomaterials having different size and stabilizing agents with various receptors. This review helps in understanding the structural features of drugs/nanomaterials crucial for not only their affinity for serum albumin but also their optimum pharmacological activities.

Contents

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1. Introduction

Investigations on the interactions of drug molecules and nanomaterials with various proteins receive considerable interest in the field of chemistry, life science and clinical medicine for decades. The nature and the magnitude of these interactions influence the biosafety, delivery rate, pharmacological response, therapeutic efficacy and the design of drugs. Hence studies on these interactions help in understanding the structural features essential for the bioaffinity of drugs and nanomaterials toward the pharmacological activity [1–4]. Since serum albumin is essential in the drug delivery of vertebrates, it is the ideal model for studying the drug–protein interactions in vitro.

Optical techniques such as absorption spectroscopy, circular dichroism, ellipsometry, differential light scattering, Raman spectroscopy, and fluorescence spectroscopy are powerful tools for studying the drug–protein interactions in vitro due to their exceptional sensitivity, speed, theoretical foundations, and straightforwardness [4–7]. Among the various optical techniques, an incalculable amount of information is acquired about the structural fluctuations and the microenvironment surrounding the fluorescent labels of proteins from the measurements and analyses of fluorescence spectra, fluorescence lifetime, fluorescence polarization, etc. Hence, fluorescence spectroscopy plays a pivotal role in the investigation of interactions between the drug molecule and the receptor (serum albumins). In particular, fluorescence quenching studies are widely utilized for revealing the accessibility of a drug/nanomaterial (quencher) to the fluorophore moiety in a protein, which in turn helps us to understand the nature and the underlying mechanism of drug–protein interactions [8].

Here we review the recent literature about the interactions of human and bovine serum albumins (HSA and BSA) with various drug molecules and nanomaterials studied using fluorescence spectroscopy. The review is organized as follows. Description about (i) HSA and BSA which are essential in the drug delivery; (ii) pivotal role of fluorescence quenching studies in determining the interactions and binding of drugs with HSA/BSA; (iii) the biological applications of metal, semiconductor and metal-doped nanoparticles, and their binding capability toward serum albumins; and (iv) the binding capability of various organic molecules such as antibiotics, anticancer drugs, anti-inflammatory agents, dyes, flavonoids and noxious materials toward serum albumins.

This review does not seek to provide an absolute review of all articles published on drug–serum albumin interactions, rather it provides a snapshot of the assortment of fluorescence quenching studies involving the interactions and emphasizes on some of the key research directions and paradigms emerging in this area.

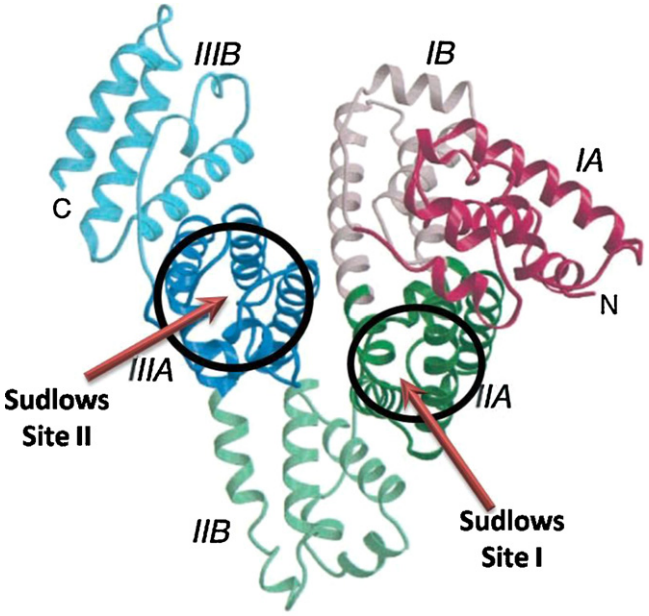

Fig. 1. The crystal structure of HSA. The domains are color-coded as follows: *red*, domain I; *green*, domain II; *blue*, domain III. The A and B sub-domains within each domain are depicted in *dark* and *light shades*, respectively.
From Ref. [9].

2. Serum albumins

Serum albumins, the most abundant soluble protein in the systemic circulation comprising 52–60% in plasma, are synthesized by the parenchymal cells of the liver and exported as a non-glycosylated protein. They possess a half life in circulation of 19 days. Serum albumins consist of amino acid chains forming a single polypeptide with well-known sequence, which contain three homologous α-helices domains (I–III) that assembled to form a heart shaped molecule whose dimensions are 80 Å × 80 Å × 80 Å × 30 Å. Each domain contains 10 helices and is divided into anti-parallel six-helix and four domains (A and B) extensively cross-linked by disulfide bridges. Fig. 1 shows the crystal structure of HSA illustrating I–III domains [9]. Serum albumins are clearly an extraordinary globular protein molecule of manifold biological and pharmacokinetic functions. They are capable of bind reversibly with a large variety of relatively insoluble endogeneous and exogeneous ligands even though their principal function is to transport metabolites such as nutrients, hormones, fatty acids and a variety of pharmaceuticals. Apart from an important role in maintaining colloidal osmotic pressure in blood, serum albumins can play a dominant role in the drug disposition and efficacy since it increases the apparent solubility of hydrophobic drugs in the plasma [9–14]. Serum albumins serve as the depot for the interacting bioactive substance and also it can be circulated through the system in the body. The binding affinity of any substance to serum