Investigation of the behavior of HSA upon binding to amlodipine and propranolol: Spectroscopic and molecular modeling approaches

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1. Introduction

The binding of a drug to a protein, or generally to a biopolymer, is governed by molecular interactions. It is generally understood that absorption, distribution, metabolism and elimination of drugs, i.e. the therapeutic effects of drugs, depend severely on these interactions [1,2]. Thus, the characterization and optimization of molecular interactions between the protein and the drugs provides important clues for the design of effective drugs for the treatment of disease. Different methods have been reported in the literatures for investigating drug binding to protein [3], among them spectroscopic techniques are relatively more sensitive and easy to use. 

This work is concerned with the association reaction between HSA and two drugs: amlodipine and propranolol. Human serum albumin (HSA) is the most abundant protein and the most extensively studied and is one of the proteins responsible for binding to and transport of numerous endogenous and exogenous compounds, such as hormones, fatty acids, metal ions and drugs. HSA has an important role in drug pharmacokinetics and pharmacodynamics due to its ability to bind to a large variety of drugs [4–8]. HSA contains three homologous helical domains (I–III), and each one can be divided into A and B subdomains. X-ray measurements have shown that the ligand binding to HSA occurs at hydrophobic cavities located in subdomains IIA and IIIA, and also at one tryptophan residue (Trp214) belonging to subdomain IIA [9,10].

Studying the interaction of drugs with HSA is of the considerable importance in that understanding of the process of drug transportation and the prediction of free drug concentration in blood serum will greatly depend on these interactions.

Amlodipine besylate (Norvasc) (Scheme 1), chemically described as 3-ethyl-5-methyl (±)-2-[(2-aminoethoxy)methyl]-4 -(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5-pyridinedicarboxylate monobenzenesulphonate, is a calcium channel blocker with highly potent vasodilating activity, used for the management of hypertension, angina pectoris and cerebrovascular disease [11,12]. Propranolol (Inderal) (Scheme 1) [1-isopropylamino-3-(1-naphthoxy)-2-propanol] is an important β-adrenergic blocking agent, prescribed in the management of hypertension, angina pectoris and cardiac dysrhythmias [13,14].

Here, the interaction between amlodipine and propranolol and HSA in aqueous solutions at physiological conditions has been investigated using spectroscopic methods - fluorescence, UV absorption and circular dichroism (CD) - along with the