

Drug-protein interactions: binding of serotonin and arachidonyl serotonin to α -lactoglobulin

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Background and Aims: α -Lactoglobulin (α -LG) is the major whey protein of cow's milk and the milk of other mammals. The biological function of α -LG is not clear, but its potential role in carrying fatty acids and drugs has been suggested. α -LG has been found in complexes with lipids and has a high affinity for a wide variety of compounds. Serotonin (5-hydroxytryptamine, 5-HT), an important drug found in animals and plants, has various functions, including the regulation of mood, appetite, sleep, muscle contraction, and learning. In this study, the interaction of serotonin and arachidonyl serotonin (AA-5HT), with α -LG was investigated using circular dichroism (CD) and fluorescence intensity measurements.

Methods: The fluorescence of 5-HT or AA-5HT was measured at 10 or 40 μ M in the presence of various concentrations of α -LG. These spectra were recorded from 310 to 450 nm with an excitation wavelength of 300 nm. Far-UV (190–260 nm) and near-UV (250–320 nm) CD spectra were obtained at a constant protein concentration of 10 μ M and 20 μ M, respectively, titrated with 5-HT or AA-5HT reaching different concentrations.

Results: It has been found in this study that these two drugs interact with α -LG forming equimolar complexes. The binding constant for the serotonin/ α -LG interaction is between 10^5 and 10^6 M⁻¹, whereas for the AA-5HT/ α -LG complex it is between 10^4 and 10^5 M⁻¹ as determined by measurements of either protein or drug fluorescence. The observed binding affinities were higher in hydroethanolic media (25%EtOH). According to far- and near-UVCD results, these drugs have no apparent influence on α -LG secondary structure, however they partially destabilize its tertiary structure.

Conclusions: The binding of serotonin and its derivative by α -LG may be one of the peripheral mechanisms of the regulation of the content of serotonin and its derivatives in the bowel of milk-fed animals.

Keywords: α -lactoglobulin; Serotonin; Binding constant; Circular dichroism