Binding of Sibutramine to Albumin is Enhanced With Caffeine

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Sibutramine is an orally administered agent for the treatment of obesity as an appetite suppressant, through the reuptake of serotonin, norepinephrine and dopamine neurotransmitters. The compound binds around 97% of serum proteins, among them serum albumin plays a major role in drug transport. In this work we studied the plausible interaction of sibutramine hydrochloride monohydrate to albumin (BSA), in the presence of caffeine, a xanthine alkaloid that acts as a psychoactive stimulant drug. Sibutramine (5-40 mM) and caffeine (10-50 mM) was incubated in the presence of 3.5 mM BSA in 50mM phosphate buffer pH 7.45 from 5 to 60min. UV-difference spectra for the interaction was followed and the results obtained by data transformation of binding isotherms and Dixon plot. A time-dependent sigmoidal trend in Langmuir isotherm was obtained at 240nm both in absence and presence of caffeine, with two non-interacting binding sites (n=1.4) and an apparent association constant of 108.7±1 mM. The apparent activation constant for caffeine was 115±2mM (93.8mM). A first-degree exponential function applied to the data (40mM sibutramine, no caffeine, 60min incubation) showed a time constant for the absorbance decay of 54.9±5.3min^{-1}. These results suggested an enhacement of sibutramine binding to albumin in the presence of caffeine.

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