HISITIDINE-146 MAY PLAY AN IMPORTANT ROLE IN N-B TRANSITION OF ALBUMIN

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Human serum albumin (HSA) is known to undergo conformational change called neutral-to-base (N-B) transition, which is known to affect the ligand binding property of HSA. We have previously reported that His146 might involve in fatty acid regulated allosteric binding of ketoprofen (KP). Thus, this prompted us to examine the involvement of His146 in N-B transition since fatty acids were reported to induce similar conformational change in HSA. Native HSA and the mutant H146I were photolabeled with [¹⁴C] KP at pH 6.0, 7.4 and 8.2. We previously found that the 11.6 kDa fragment contains subdomains IIIA and IIIB, the common binding region for site II, and the 9.4 kDa band contains subdomain IA. The 11.6 kDa and 9.4 kDa fragments of HSA but only 9.4 kDa fragment of the mutant contained most of the photoincorporated radioactivity. The extents of incorporated radioactivity of 11.6 kDa under different pHs were comparable but 9.4 kDa band showed an increased radioactivity with increasing pH for HSA. Interestingly, it is noteworthy that the extent of radioactivity for the 11.6 kDa as well as the 9.4 kDa bands of the mutant were almost the same under all pHs examined. These results clearly indicate that the ligand binding region contained in 11.6 kDa fragment may be pH independent but that in the 9.4 kDa fragment is sensitive to pH and conformational change. The above results suggest that His146 may be a key amino acid residue involved in N-B transition.