

Photochemical Reaction of Ketoprofen with Twenty Kinds of Proteinogenic Amino Acids

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Ketoprofen (KP) is one of the most popular nonsteroidal anti-inflammatory drugs, however, drug-induced photosensitivity of KP has been reported as a serious side effect. KP is incorporated into a protein, and a covalent bond is formed between KP and a protein via the generation of free radicals by irradiation of UV light, which leads to production of an allergen¹⁾. The photochemistry of KP with twenty kinds of proteinogenic amino acids in the phosphate buffer solution at pH 7.4 was studied by transient absorption spectroscopy. KP carboxylate anion (KP[−]) gave rise to a carbanion via a decarboxylation within a nanosecond, and the carbanion yielded 3-ethylbenzophenone ketyl biradical (3-EBPH) through a proton transfer reaction²⁾. Twelve kinds of proteinogenic amino acids obviously accelerated the reaction. The reaction rate constant to form 3-EBPH with each amino acid was successfully determined. In addition, structural information on the complexes of KP[−] docked in a human serum albumin (HSA) was obtained by molecular mechanics (MM) and molecular dynamics (MD) calculations. From the reactivity of the KP carbanion with proteinogenic amino acids and the stable structures for the complexes of KP[−] docked in a HSA, the initial processes of photochemical reaction of KP[−] in a HSA were discussed. The approach in this work would be the effective for understanding of the mechanism for drug-induced photosensitivity of other NSAIDs.

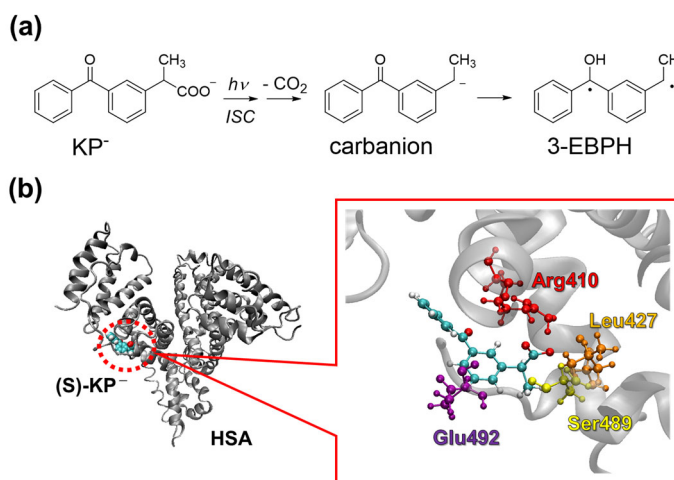


Fig. 1 (a) Reaction scheme of KP carboxylate anion (KP[−]) with UV irradiation. (b) Most stable structure of complex of (S)-KP[−] docked in a HSA.

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