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Deproteinization with $ZnSO_4$-$Ba(OH)_2$ reduces the photodegradation of montelukast in plasma during bioanalysis

Eunjeong Shin[a], Ju-Hee Oh[a], Joo Hyun Lee, and Young-Joo Lee[a,b,*]

[a]Division of Biopharmaceutics, College of Pharmacy, Kyung Hee University, Seoul, 130-701, Korea

[b]Department of Life and Nanopharmaceutical Sciences, Kyung Hee University, Seoul, 130-701, Korea

*E-mail: yj_lee@khu.ac.kr

Montelukast (MKT) Sodium ($C_{35}H_{35}ClNNaO_3S$) (Fig. 1) is a leukotriene receptor antagonist used in the maintenance treatment of asthma as well as to relieve symptoms of seasonal allergies [1]. MKT is a light-sensitive compound, and if exposed to light, degrades into MKT cis-isomer, MKT S-oxide, and MKT dehydrogenate (Fig. 1) [2]. Thus, in the current study, we quantified the stability of MKT in plasma compared to that in water and developed a simple method to minimize analytical error caused by photodegradation during the bioanalysis of MKT. For the latter purpose, we optimized the deproteinization process for plasma samples, because it is an essential, but time-consuming, step in the analysis of biological fluids, which has a high risk of light exposure. We evaluated the stability of MKT in water and plasma in real time using HPLC, and optimized a sample deproteinization procedure by investigating the effectiveness of different deproteinization solutions.

When exposed to light, MKT is quickly photodegraded in water, and to a lesser extent in plasma; 55% of the MKT in plasma was degraded within 2 hours. Deproteinizing the plasma samples using $ZnSO_4$-$Ba(OH)_2$ dramatically reduced the photodegradation of MKT, while precipitation using methanol or acetonitrile accelerated photodegradation.

In this study, we confirmed that rapid photodegradation of MKT occurs in plasma samples. Proper protection from light is required for the bioanalysis of MKT. Interestingly, common precipitation methods using methanol or acetonitrile accelerate the photodegradation of MKT, while $ZnSO_4$-$Ba(OH)_2$ dramatically improves the photostability of MKT. These findings can be applied successfully to generate precise pharmacokinetic evaluation of MKT such as in bioequivalence studies.

Keywords: Montelukast; Light-sensitive; Deproteinization; Plasma; Pharmacokinetics

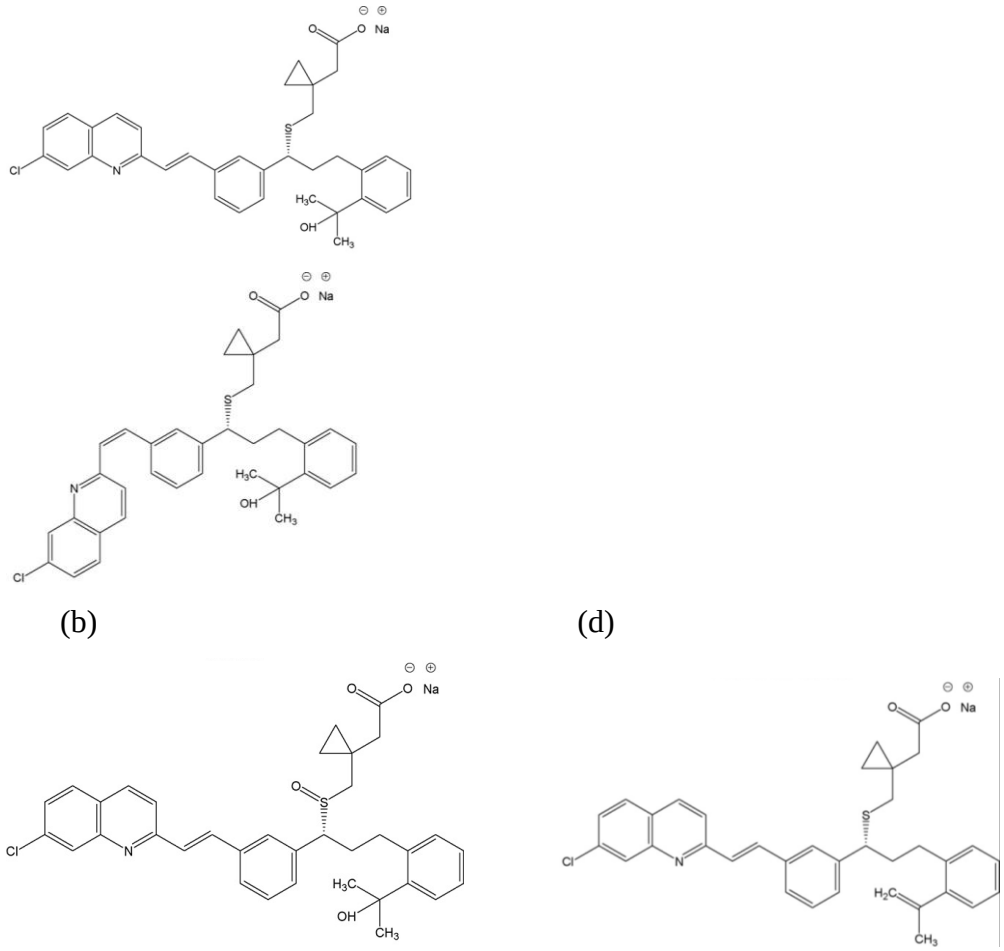

Fig.1. Chemical structures of Montelukast and its known photoproducts: (a) MKT, (b) MKT cis-isomer, (c) MKT S-oxide, (d) MKT dehydrogenate

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