Archives of Pharmacy Practice
Abstract Conference Proceedings
2nd Asia Pacific Pharmacy Education (PharmED) Workshop
ISSN 2045-080X Vol. 3, Issue 1, 2012

DP-031

COMPARISON OF THE VKOR INHIBITORY ACTIVITIES BY *S*- AND *R* -WARFARIN

Masashi Kawano[1], Takuya Araki[1], Tomonori Nakamura[1,2] and Koujirou Yamamoto[1,2]

[1]Department of Clinical Pharmacology, Gunma University Graduate School of Medicine, 3-39-22 Showa-machi, Maebashi 371-8511, Japan

[2]Departmant of Pharmacy, Gunma University Hospital, 3-39-15 Showa-machi, Maebashi 371-8511, Japan

*E-mail: m10701005@gunma-u.ac.jp

ABSTRACT

Warfarin inhibits the vitamin K epoxide reductase (VKOR) which is a key enzyme of the vitamin K (VK) recycle and is widely used as an oral anticoagulant. Warfarin is clinically administered as a racemic mixture of *S*- and *R*-warfarin. Although the anticoagulation activity of *S*-warfarin is known to be around 5-fold stronger than that of *R*-warfarin in clinical setting, the difference of VKOR inhibitory activities of them has not entirely clarified. Thus, we assessed the difference of VKOR inhibitory activities of warfarin enantiomers. Reaction mixtures containing 1 mg/mL of human hepatic microsome, 10 μM of VK_2 epoxide and 1 nM to 200 μM of *S*- or *R*-warfarin were pre-incubated for 5 min at 37°C. The reaction was initiated by addition of DTT, followed by incubation for 20 min at 37°C as metabolic reaction and the amount of VK_2 product was determined by HPLC method. IC_{50} values of warfarin enantiomers for VKOR were determined by fitting the concentration of VK_2 versus warfarin concentration to linear regression analysis. The IC_{50} values of *S*-warfarin was around 6-fold stronger than that of *R*-warfarin (0.56 and 3.2 μM, respectively). However, the inhibition rate at the concentration of clinical use of *S*- (1 μM) and *R*-warfarin (3 μM) were 65.2% and 43.8%, respectively. Our results suggest that while the potential inhibitory activity of *S*-warfarin is much higher than that of *R*-warfarin, the inhibition activity of *S*-warfarin in clinical setting may be not higher than that of *R*-warfarin as reported previously.