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Chronic effect of Neurostan on the hepatic disposition of Fexofenadine in the isolated perfused rat liver

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Abstract

The overall purpose of this study was to investigate Neurostan Saint John's Wort (SJW) on the disposition of fexofinadine in the isolated perfused rat liver. Sprague-Dawley (SD) rats (n = 16) randomized into 3 groups, including: control, low dose (Hypericum, one type of neutostan) and high dose group. Each animal among these groups was pre-treated with either vehicle (ethanol in Milli Q water at 16 μg/ml) or low dose hypericum (150 mg/kg/day) or high dose hypericum (500 mg/kg/day), respectively for 14 consecutive days via gastric gavage. The administration volume was 1 ml/100g for all animals. Each rat liver was isolated and perfused in a recirculating system with medium containing fexofenadine at an initial concentrateion of 2000 ng/ml. The total amount (ng) of fexofenadine excreted into bile for the control vs. the low dose vs. the high dose group, was 141678 ± 32351, 165270 ± 37340 and 222842 ± 22996* respectively, and the fexofenadine biliary clearance (ml/min) was 4.226 ± 0.955, 4.855±1.961 and 8.567 ± 2.323* respectively. Although, the ratio of liver to perfusate (L/P) was not significantly different, the ratio of bile to liver concentration (B/L) for the high dose group (1.59±0.87*) was notably higher than that for the control group (0.82±0.36). All together, it can be concluded that neurostan increases the hepatic p-glycoprotein (p-gp) thus raising the biliary cleara-nce and the B/L ratio of the substrates (fexofenadine) transported by p-gp.

Key words: Keywords: Neurostan; P-glycoprotein (p-gp); Fexofenadine, Liver

Introduction

Saint John's Wort (SJW) is a complementary drug used in treating anxiety and depression, and several placebo-controlled clinical studies already confirmed its antidepressant effect (Capasso, Borrelli, Montanaro, Altieri, Capasso, & Izzo, 2005; Durr, Stieger, Kullak-Ublick, Rentsch, Steinert, Meier, & Fattinger, 2000). Neurostan, one of the most popular brand mainly containing SJW, is usually used in combination with other drugs such as fexofenadine. It was reported that SJW increased the expression of p-glycoprotein (p-gp) and

