

Metabolic Enzymes and Patient Variability Influence on the Bioequivalence of Bupropion

Bupropion is a clinically available drug product used for depression and smoking cessation. Generics of Wellbutrin extended release (XL) were approved based on bioequivalence (BE) studies comparing the 150 mg strength of the products to Wellbutrin XL 150 mg. The results were extrapolated to establish bioequivalence of the 300mg product. However, BE studies for 300 mg XL showed bioinequivalence for some generics. The purpose of these studies is to understand how metabolism/ metabolic enzymes expression and release rates formulation influences bupropion pharmacokinetics. Bupropion produces three active metabolites via two separate pathways, Cytochrome P450 2B6 and Carbonyl Reductase. In the first study, we compared the relative contribution of the two metabolism pathways of bupropion (by CYP2B6 and carbonyl reductase) in the subcellular fractions of liver and intestine, investigated the difference of bupropion's metabolism in both liver and intestines, and to identified carbonyl reductases responsible for bupropion's metabolism in the liver and the intestine. In the second study, we are looking at healthy individuals to see how both enzyme expression differences (polymorphism in CYP2B6) and release rates from formulations (immediate, sustain, or extended release) can affect the pharmacokinetics of bupropion and metabolites.