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TITLE

LIVER DISEASES AFFECTING BIOAVAILABILITY

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The liver is the major body site for xenobiotic metabolism, the biotransformation of chemicals not normally present in biological systems, such as environmental pollutants and medications. It determines the disposition of many drugs. The plasma concentration of unchanged drug is directly affected by the liver metabolism. Drugs with high lipophilicity and pKa undergoes extensive first pass metabolism, adversely affecting the therapeutic action. There are two determinants to a drugs therapeutic efficacy, namely, its intrinsic activity at a target and its bioavailability at the site of action. Liver disease causes multiple pathophysiologic changes that influence drug bioavailability. Decreased hepatic blood flow, extrahepatic and intrahepatic blood shunting, and loss of hepatocytes alter the ability to metabolize drugs. The bioavailability of administered medications increases, effectively increasing the dose. Decreased protein synthesis decreases the percentage of drug bound to plasma proteins and increases the amount of "free" or unbound drug. The increase in free fraction makes more drug available to the receptor site and more drug available for metabolism, thereby increasing its clearance. Increased clearance does not occur if hepatocytes are not capable of metabolizing the drug, however. An increase in free fraction and a decrease in hepatocyte function result in an increase in free drug concentration.There is a significant potential for liver disease to alter the pharmacokinetics as well as pharmacodynamics of many drugs.