the fraction of the oral dose that reaches systemic circulation to be bioavailable (Leucuta and Vlase 2006). Phase I reactions include the following:

Oxidation

Oxidation process involves the addition of oxygen or the removal of hydrogen from the parent molecule which is a common type of phase I reaction. There is an extensive system of enzymes that are capable of catalyzing oxidation reactions, such as cytochrome P-450 reductase. Examples of microsomal oxidation reactions are aromatic oxidations (e.g., PRN, warfarin), aliphatic oxidations (e.g., amobarbital, ibuprofen), O-dealkylations (e.g., codeine), N-dealkylations (e.g., morphine), S-dealkylations (e.g., 6-methylthiopurine), epoxidations (e.g., carbamazepine), S-oxidations (e.g., cimetidine); N-oxidations of primary amines (e.g., chlorphentermine), secondary amines (e.g., acetaminophen) and tertiary amines (e.g., nicotine); in addition to deaminations (e.g., diazepam).

Other non-P450 oxidations are: Alcohol- and aldehyde dehydrogenase, tyrosine hydroxylase, xanthine oxidase and monoamine oxidase reactions, such example is the formation of imine followed by hydrolysis, such as flavin monooxygenase reactions (FMO). P450 reductases also use flavin as flavin adenine dinucleotide (FAD), and flavin mononucleotide (FMN) (Leucuta and Vlase 2006; Raffa 2010).

Reduction

Reduction reactions involve the addition of hydrogen or the removal of oxygen from the parent drug; it occurs in both microsomal and nonmicrosomal fractions of hepatocytes and other cells. Examples of such reactions include, aldehyde-, ketone-, nitro-, azo-, and quinone reduction (Raffa 2010).