Contents

Chapter 1  
General introduction and aim of this thesis

Chapter 2  
Generic method for the absolute quantification of glutathione S-conjugates: application to the conjugates of acetaminophen, clozapine and diclofenac

Chapter 3  
Characterization of cytochrome P450 isoforms involved in sequential two-step bioactivation of diclofenac to reactive p-benzoquinone imines

Chapter 4  
Simulation of inter-individual differences in inactivation of reactive para-benzoquinone imine metabolites of diclofenac by glutathione S-transferases in human liver cytosol

Chapter 5  
Cytochrome P450 mediated bioactivation of mefenamic acid to quinoneimine intermediates and inactivation by human glutathione S-transferases

Chapter 6  
Reduction of chemically reactive drug metabolites by NAD(P)H:quinone oxidoreductase 1 and NRH:quinone oxidoreductase 2 and variability in hepatic concentrations

Chapter 7  
Inter-individual variability in activity of the major drug metabolizing enzymes in liver homogenates of 20 individuals

Chapter 8  
Variability in hepatic cytochrome P450 mediated formation and glutathione S-transferase catalyzed detoxification of clozapine and diclofenac derived reactive metabolites in liver homogenates of 20 individuals

Chapter 9  
Summary, conclusions and future perspective

Appendices
1. List of abbreviations
2. Nederlandse samenvatting
3. List of publications
4. Curriculum Vitae
5. Acknowledgements