## Contents

**PART I**  INTRODUCTION  
Chapter 1  General introduction  9

**PART II  YEAST AS A CELLULAR MODEL TO STUDY DRUG METABOLISM AND METABOLISM-RELATED TOXICITY**  
Chapter 2  Metabolism related toxicity of diclofenac in yeast as model system  41  
Chapter 3  Reconstitution of the interplay between cytochrome P450s and human glutathione S-transferases in clozapine metabolism in yeast  57

**PART III  FORMATION AND DETOXIFICATION OF (REACTIVE) DRUG METABOLITES USING RECOMBINANT ENZYMES**  
Chapter 4  Human NAD(P)H:quinone oxidoreductase 1 (NQO1)-mediated inactivation of reactive quinoneimine metabolites of diclofenac and mefenamic acid  79  
Chapter 5  Activation of the anticancer drugs cyclophosphamide and ifosfamide by cytochrome P450 BM3 mutants  101  
Chapter 6  Selective whole-cell biosynthesis of the designer drug metabolites 15- or 16-β-hydroxynorethisterone by engineered cytochrome P450 BM3 mutants  121

**PART IV  CONCLUSIONS**  
Chapter 7  Summary, conclusions and perspectives  153  
Appendices:  
Nederlandse samenvatting  166  
List of publications  170  
Curriculum Vitae  171  
Dankwoord  172