# Table of Content

1. Small Active Molecules with Insulin Mimetic Activity  
   *Muhammad Taher*  
   
2. Liver and Kidney Protective Effects of the Polyphenols, Tocopherols and Carotenoids  
   *Julliana bt Md. Jaffri*  
   
3. Potential Surface Active Properties of *Nigella sativa*  
   *Siti Nurfaajarziah bt Said and Kausar bt Ahmad*  
   
4. Pufa in Fish: Extraction and Fractionation Methods  
   *Sahena Ferdosh and Md. Zaidul Islam Sarker*  
   
5. Polypyrrole-Peg Composite Film for Drug Delivery  
   *Khadijah bt Eduweng*  
   
6. Co-Encapsulation of Cyclophosphamide and Mesna into Double-Walled Microspheres  
   *Farahidah bt Mohamed and Christopher van der Wallle*  
   
7. A Recent Updates of Polysaccharide Based Nanoparticulate Oral Preparation of Insulin with Special Emphasis on *In Vivo* Application  
   *Uttam Kumar Mandal*  
   
8. Development of an Appropriate and Robust Dissolution Method for Solid Dosage Forms  
   *Uttam Kumar Mandal*  
   
9. Use of Cyclodextrin in the Production of Biomedical Nano Particles  
   *Omar El-Hadad*  
   
10. The Role of Pharmacogenetic Variation in Metoprolol CYP2D6 Genotypes Polymorphism  
    *Wan Mohd Azizi Wan Sulaiman, Tariq Abdul Razak, Lay Kek Teh and Rusli Ismail*  
    
11. Polymorphic Crystals and Their Characterisation  
    *Mohd Rushdi Abu Bakar, Zoltan Kalman Nagy and Christopher David Rielly*  
    
12  

37  

51  

64  

77  

97  

116  

126  

133  

163
CHAPTER 10

THE ROLE OF PHARMACOGENETIC VARIATION IN METOPROLOL CYP2D6 GENOTYPES POLYMORPHISM

Wan Mohd Azizi Wan Sulaiman1, Tariq Abdul Razak1, Lay Kek Teh2 and Rusli Ismail3

1Kulliyyah of Pharmacy, International Islamic University Malaysia, Jalan Istana Bandar Indera Mahkota 25200 Pahang, Malaysia
2Pharmacogenetics Research Group, Faculty of Pharmacy, Universiti Teknologi MARA, 40450 Selangor, Malaysia
3Pharmacogenetics Research Group, Institute for Research in Molecular Medicine, Universiti Sains Malaysia, 16150 Kelantan, Malaysia

Ticlopidine is used as an anti-platelet in patients with ischaemic heart disease. An in vitro study suggested that ticlopidine inhibited CYP2D6 and the widely used antianginal metoprolol is metabolized by this polymorphic enzyme. The objective of this study was therefore to investigate the effect of ticlopidine treatment into patients maintained on chronic metoprolol therapy. The study was approved by the Ethics Committee of International Islamic University Malaysia (IIUM) and strictly adhered to Malaysian Good Clinical Practice (GCP) guidelines. This was an open labelled Case Controlled Study where all the patients were screened for the inclusion/exclusion criteria. CYP2D6 genotyping were performed for *3,*4,*5,*6,*9,*10, *14, *17 and duplication. Two weeks after the screening visit, blood for metoprolol was taken at timed intervals together with serial measurement on blood pressures and heart rates. Subsequently the patients were given a standard dose of ticlopidine 250 mg twice daily for a period of one month. At the end of study period, blood for metoprolol was repeated together with serial measurement on blood pressures and heart rates. After 18 months, 87 patients completed the study. From our study, it was showed that the frequency of predicted Poor Metabolizer (PM) was low at 2.6%, where both patients had homozygous *4/*4 and majority of them (47.8%) belong to the allele *10, predicted Intermediate Metabolizer (IM). After ticlopidine treatment, there were increasing