

Pharmaceutical Technology Perspectives

Muhammad Taher



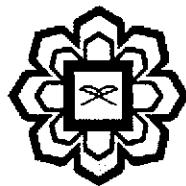
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Editor

Muhammad Taher



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Table of Content

1. Small Active Molecules with Insulin Mimetic Activity	12
<i>Muhammad Taher</i>	
2. Liver and Kidney Protective Effects of the Polyphenols, Tocopherols and Carotenoids	25
<i>Juliana bt Md. Jaffri</i>	
3. Potential Surface Active Properties of <i>Nigella sativa</i>	37
<i>Siti Nurfajariah bt Said and Kausar bt Ahmad</i>	
4. Pufa in Fish: Extraction and Fractionation Methods	51
<i>Sahena Ferdosh and Md. Zaidul Islam Sarker</i>	
5. Polypyrrole-Peg Composite Film for Drug Delivery	64
<i>Khadijah bt Edueng</i>	
6. Co-Encapsulation of Cyclophosphamide and Mesna into Double-Walled Microspheres	77
<i>Farahidah bt Mohamed and Christopher van der Wallle</i>	
7. A Recent Updates of Polysaccharide Based Nanoparticulate Oral Preparation of Insulin with Special Emphasis on <i>In Vivo</i> Application	97
<i>Uttam Kumar Mandal</i>	
8. Development of an Appropriate and Robust Dissolution Method for Solid Dosage Forms	116
<i>Uttam Kumar Mandal</i>	
9. Use of Cyclodextrin in the Production of Biomedical Nano Particles	126
<i>Omar El-Hadad</i>	
10. The Role of Pharmacogenetic Variation in Metoprolol CYP2D6 Genotypes Polymorphism	133
<i>Wan Mohd Azizi Wan Sulaiman, Tariq Abdul Razak, Lay Kek Teh and Rusli Ismail</i>	
11. Polymorphic Crystals and Their Characterisation	163
<i>Mohd Rushdi Abu Bakar, Zoltan Kalman Nagy and Christopher David Rielly</i>	

CHAPTER 10

THE ROLE OF PHARMACOGENETIC VARIATION IN METOPROLOL CYP2D6 GENOTYPES POLYMORPHISM

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*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*