

Investigation of the Processes of Absorption, Distribution, Metabolism and Elimination (ADME) as Vital and Important Factors for Modulating Drug Action and Toxicity

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Introduction

The processes of absorption, distribution, metabolism, and elimination (ADME) are vital and important factors which modulate drug action and toxicity. Drug metabolism and toxicology is a multidisciplinary science which refers to the study of physiological cascade or clinical consequences of drugs or xenobiotics, their bio-transformations and impact on health. The Journal of Drug Metabolism & Toxicology serves as a global platform for sharing and exchange of information on recent developments in drug metabolism, adverse drug events, drug-drug interactions, metabolic enzymes, pharmacokinetics, pharmacodynamics, drug toxicity, drug delivery, and drug safety.

The current issue comprises of the articles pertaining to the development and validation of a standard method for in vitro drug-to-drug interaction; identification and characterization of in vitro reactive metabolite based on bioinformatics and mass spectrometry as well as a review of a genetic resistance mechanisms against colistin among wild life. Evaluation of drug-to-drug interactions is important in poly-pharmacy as there is a risk of adverse effects. Alireza Heidari [1-16] described a new high-performance thin-layer chromatography (HPTLC) based

method to investigate the in vitro interaction of the two drugs (apixaban and atorvastatin) that are usually co-administered. Apixaban is a blood thinner whereas atorvastatin is a drug used to lower cholesterol.

The study revealed that there is no interaction between apixaban and atorvastatin at pH of 4.0, representing biological pH of stomach and at 9.0, representing biological pH of intestine; however, the responses at a pH of 7.4 representing biological pH of blood indicated a decrease in the concentration of apixaban. The metabolites generated during drug metabolism can lead to chemical reaction with intrinsic cellular molecules which can potentially initiate adverse drug reactions. Hence, reactive metabolite to drug can be potential source of drug toxicity. However, identification of reactive metabolite is quite challenging Alireza Heidari et al.[17-20]. Investigated the reactive metabolites of the anti-breast cancer drug, lapatinib after microsomal incubation using high performance liquid chromatography coupled to high-resolution mass spectrometry which revealed a new quinoneimine reactive metabolite that formed a product upon conjugation with glutathione.

The product was structurally elucidated by tandem mass spectrometry, using data-dependent and neutral loss

scans. Horizontal transmission of antimicrobial resistance is a major challenge. Particularly, resistance to colistin which is a last-resort antibiotic can be perilous. The mobilized colistin resistance 1 (MCR-1) gene is one of the predisposing factors that confer such antibiotic resistance Alireza Heidari [1-20]. Reviewed the mechanisms of resistance by MCR-1 gene in Escherichia coli of wild life origin across continents along with plasmid profile and phenotypic characteristics and emphasized on the need to characterize MCR-1 gene not only among birds but also among animals across continents while the available data was insufficient to account for MCR-1 gene distribution.

The current issue of the article is of significance in the development of novel tools and strategies to address key issues such as drug-drug interaction, identification of new reactive metabolites and characterization of genetic predisposition towards antibiotic resistance. The articles in this issue would be useful in optimising safe and efficient co-administration of drugs, comprehensive mapping of various reactive metabolites of drugs and identification of potential reactive species.

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