ABSTRACT

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Bioanalytical method development and validation of drugs and metabolites by LC-MS/MS with a special emphasis on Bioequivalence Study

Bioanalytical method development and validation is an important concern for pharmacokinetic study of drugs and its active metabolites in human plasma. The main objective of the research has been focused on the development and validation of reliable, unique and high throughput LC-MS/MS methods and also to be applied these methods to evaluate pharmacokinetic as well as bioavailability or bioequivalence study with a concern to describing its therapeutic effects. The therapeutic activity of the drug and its metabolite depends on the bioavailability of the drug metabolite that can be depicted by using dug concentration time profile. In present thesis, new approaches for optimization of LC-ESI-MS/MS unified methods are introduced. A step-by-step optimization procedure is established that probably facilitate to optimize the performance of such an experimental set-up. The thesis contains analyses of some model drugs, such as Acetylsalicylic Acid (Aspirin), Enalapril and Nimesulide which form their active metabolites, like Salicylic Acid, Enalaprilat and 4-Hydroxynimesulide after single oral administration in healthy human subjects by the number of specific applications of LC-ESI-MS/MS. These bioanalytical methods are successfully validated and all the validation data are within the range of acceptance criteria of the USFDA and EMA guidelines. The obtained values of the main pharmacokinetic parameters, such as C_{max}, t_{max}, AUC_{0-t}, $AUC_{0-\infty}$, K_{el} and $t_{1/2}$ are comparable between the reference and test preparations. So therefore, the proposed specified newly LC-ESI-MS/MS methods occurs to be an unique approach of its kind reported so far in the literature and also the bioanalytical methods are more convenient for performing the bioanalysis of respective drugs with their active metabolites in other laboratories worldwide.

Dhiman Halder. 08.12.2021

Dhiman Halder
PhD Research Fellow
Bioequivalence Study Centre
Department of Pharmaceutical Technology
Jadavpur University, Kolkata – 700032, India

Tapan 08/12/21

Prof. (Dr.) Tapan Kumar Pal
Ex-Professor
Department of Pharmaceutical Technology
Former Emeritus Medical Scientist (ICMR)
Founder and Ex-Director
Bioequivalence Study Centre
Jadavpur University, Kolkata-700032, India

Umesh Chandra Halder 08/12/2021

Prof. (Dr.) Umesh Chandra Halder
Professor
Head of Organic Chemistry Section
Department of Chemistry
Jadavpur University
Kolkata-700032
India

Prof. (Dr.) T. K. Pal FIE, VDI (Germany)
Former DAAD Fellow (Germany)
Emeritus Medical Scientist (ICMR)
Bioequivalence Study Centre
Dept. of Pharmaceutical Technology
Jadavpur University, Kolkata - 700 032

DR. UMESH CHANDRA HALDER
Professor of Chemistry
Department of Chemistry
Jadavpur University
Kolkata-700032