Bioavailability testing of drug products in animals and humans provides the most appropriate method available for determining the drug in the body. The design, performance, and evaluation of Bioavailability studies have received major attention from academia, the pharmaceutical industry and health authorities over the last couple of decades. Hence the focus of the research is to develop suitable bioanalytical methods for selected drugs Bosentan, Flecainide, Betahistine and Budesonide in plasma samples. This research has contributions in 3 important scientific fields. From a bioanalytical point of view, the extensive study of this novel instrumentation has resulted in innovative methodology for selected drugs in plasma samples. From a clinical and bioequivalence point of view, application of the new LC-MS/MS procedures widened our knowledge about concentration-time profiles in human plasma. From a pharmacokinetic point of view application of the concentration-time profiles by non-compartmental statistics model using WinNon-Lin 5.0 software for selected drugs broadened our knowledge in in vivo studies calculations. Hence, it is evident and will unquestionably expand future research capabilities.