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ICP-MS Coupling to HPLC to Quantify Unknown Metabolite of Drugs in Biological Fluids

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Introduction: The application of HPLC-MS/MS in pharmacokinetic studies has been extremely helpful permitting to solve complex metabolism problems; it remains however a main problem to quantify the newly identified metabolites until a quantitative standard is available. Aiming to quantitate the concentrations of unknown metabolites in absence of adequate quantitative standards, ICP-MS has been combined to HPLC and, as an example, experimental results obtained on clopidogrel, a potent antiaggregant and antithrombotic drug characterized by an extensive metabolization, are here presented.

Materials and methods: This research was carried out using triple quadrupole MS/MS systems (API-4000 and API 5000 Applied Biosystems) and a quadrupolar ICP-MS (ELAN 6100 Perkin Elmer). HPLC separations were carried out (Agilent or Perkin ELmer HPLC pumps) on reversed phase or ion exchange columns eluted with different mobile phases in gradient or isocratic conditions. HPLC-MS and MS/MS analyses were performed in positive or negative ions mode in order to get the maximum of chemical structure information; in case of ICP-MS chromatographic traces with masses characteristic of sulfur were acquired. Plasma samples collected from subjects treated orally with clopidogrel as well samples obtained by “in vitro” metabolization of clopidogrel were analyzed and compared with a few synthetic clopidogrel metabolite standards.

Results and conclusions: Results obtained using different models of HPLC-ICP interfaces and mobile phase composition will be presented. Under adequate conditions of mobile phase composition and flow rate the application of ICP-MS to HPLC proved to be an effective tool to quantify known and unknown clopidogrel metabolites.