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DEVELOPMENT AND VALIDATION OF ANALYTICAL METHODS TO DETERMINATION OF DABIGATRAN ETEXILATE IN PHARMACEUTICAL FORMULATIONS

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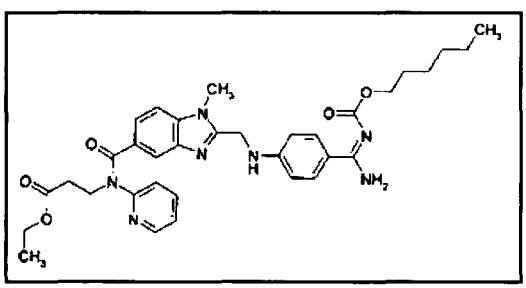
Introduction: Venous and arterial thromboembolic diseases are still the most frequent cause of death and disability in high-income countries. Antithrombotic drugs inhibiting coagulation or platelet function play a key role in the management of these patients[1]. Dabigatran (DAB) is a reversible, competitive, direct thrombin inhibitor which has shown to be an effective antithrombotic agent and to be efficacious and safe in the prevention of deep vein thrombosis in patients undergoing elective total hip or knee replacement[2]. The prodrug dabigatran etexilate (DEM) is an oral direct thrombin inhibitor rapidly converted to the active form dabigatran once absorbed from the gastrointestinal tract. It is a new drug approved for the prevention of venous thromboembolism following major lower limb orthopedic surgery[1]. In Brazil, DEM is available in the market as Pradaxa®, commercialized by the Boehringer Ingelheim. There are not references in the literature about studies of quantitative determinations and stability studies of DEM in pharmaceutical formulations.
Objective: The aim of the present work will be to develop and validate analytical methods to determine DEM in pharmaceutical formulations using liquid chromatography (LC) and capillary electrophoresis (CE) and its applications in dissolution studies. Also to perform stability studies and determination of degradation kinetics of the drug, with subsequent isolation and elucidation of the major degradation product formed.
Materials and Methods: In the selection and optimization of the LC conditions, factors including: selection of mobile phase, flow and pH, separation columns of different stationary phases, choose of the wavelength for detection, injection volume and temperature analysis will be studied. Compliance of the system as the chromatographic capacity factor, peak asymmetry, resolution of potential interferences, theoretical plates and precision of injection will be investigated. During the development of the technique for CE different experimental conditions are going to be tested and optimized considering the characteristics of the drug, the method (size and extent of fused-silica capillary, mode and time of injection, composition, concentration and pH of the electrolyte, applied voltage and temperature of analysis). The dissolution test is going to be performed in accordance with compendial methods and developed according to the solubility of the drugs to achieve an adequate condition. Therefore, the apparatus, speed of agitation, sampling and other parameters related to the dissolution medium, such as volume, pH, temperature and necessary additives are going to be analyzed. The methodologies will be validated according to ICH guidelines.
So far, the samples of pharmaceutical formulation Pradaxa® and dabigatran etexilate standard were purchased. They are available to the start the preliminary tests.
Thus, the objective is to establish procedures that can contribute to the scientific and technological field, improving the area of quality control, ensuring the safety and efficacy of pharmaceutical products.



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