SITAGLIPTIN PHOSPHATE: EVALUATION FOR CAPILLARY ELECTROPHORESIS AND PHOTODEGRADATION KINETICS STUDY.

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Introduction: Diabetes mellitus (DM) is a disease of multiple etiologies, resulting from inadequate secretion of insulin and the inability to adequately perform the same function. This disease is a serious public health problem due to its high frequency in the population, its complications, and financial and social costs involved in the treatment. The sitagliptin phosphate (STG) is the first drug of a relatively new class of drugs for the treatment of type 2 diabetes. Sitagliptin phosphate is found in the Brazilian market as Januvia®, in the form of coated tablets containing 25mg, 50mg and 100mg of the drug. The development and commercialization of the product are under the responsability of Merk Sharp & Dohme Pharmaceutical Ltda.
Objective: The aim of this study was to develop and validate a stability-indicating capillary electrophoresis method for the determination of STG in coated tablets as well as to determine the photodegradation kinetics of the drug in methanolic solution.
Materials and Methods: The STG phosphate reference standard (99.6%), and STG phosphate coated tablets containing 50 mg (free base) of STG were used in the analysis. The analysis of STG occurred in a capillary electrophoresis system HP3D - CE (Agilent) equipped with diode array UV detector. It was used a capillary with 40 cm effective length, the applied voltage was 30kV, wavelength for analysis of 207 nm, injection volume of 5s at a pressure of 50mbar (hydrodynamic injection) and the temperature of analysis was 25 °C. The electrolyte used was Tris 50mM added by SDS 75mM, solution at pH 10.6. The following analytical parameters were evaluated: specificity, linearity, precision, accuracy and robustness. The photodegradation kinetics was carried out with quartz cells containing STG phosphate in methanolic solution exposed to UVC radiation (254 nm), at pre-established times (0, 0,5, 1, 2, 3 and 4 hours).
Results and Discussion: The linearity was obtained from experiments performed in triplicate by constructing a standard curve in the average range 50-150 µg/ml. The correlation coefficient (r=0.9990) demonstrated the linearity of the method in the concentration range evaluated. The precision was assessed by repeatability and intermediate precision. The method is precise, since the relative standard deviations (RSD) evaluated by the repeatability were less than 2.0 % and intermediate precision presented a RSD of 1.83 %. The average percentage of STG was 98.80 % of the declared content. The accuracy was evaluated by recovery test using the method of standard additive. The added amounts of STG corresponded to 25, 50 and 75 % of the starting point of the curve (50 µg/ml). The method proved to be accurate by the results obtained, showing percentage of average recovery of 101.02 %. The study of possible interferences in the quantitative determination of STG was evaluated. It was found that the excipients in the formulation do not interfere in the analysis, as well as the likely degradation products formed. In the Plackett-Burman experiment, six factors were evaluated (pH, TRIS and SDS concentrations, temperature, wavelength and voltage). The responses obtained for each experiment were related to the values obtained from the coated tablet dosage form compared to a STG reference standard, analyzed under the same conditions. After calculating the effects for each parameter, the statistical interpretation, by "t" test was done. None of the factors studied were significant ($\alpha = 0.05$). The STG photodegradation kinetic rate was determined by plotting the drug concentration (zero-order process), the log (first-order process) and the reciprocal (second-order process) concentration versus time. The degradation of STG in methanolic solutions could be better described as second order kinetic ($r = 0.9830$).
Conclusions: The method developed by capillary electrophoresis was properly validated and proved to be linear, precise, accurate, specific and robust for the quantitative analysis of sitagliptin phosphate coated tablets. This method also allowed the determination of the kinetics of degradation of STG.

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