Development and validation of a Stability Indicating HPLC method for determination of Dapagliflozin in tablets

Rafaela Z. C. Meira¹, Cassiana Mendes², Marcos A. S. Silva², Larissa S. Bernardi¹, Paulo R. Oliveira¹

¹Post-Graduation program in Pharmaceutical Sciences, Department of Pharmacy, UNICENTRO, 85040-080, Guarapuava-PR, Brazil, ²Department of Pharmaceutical Sciences, Health Science Centre, Federal University of Santa Catarina, 88040-900, Florianópolis-SC, Brazil.

*rafa_zielinski@hotmail.com

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Introduction

Dapagliflozin (DAPA) is a highly potent, selective and reversible inhibitor of sodium-glucose cotransporter 2 (SGLT2) (WHITE, 2015). Its commercial formula, Forxiga®, was approved by the FDA in January 2014 and by ANVISA in July 2013 (Bristol-Myers Squibb, 2015; FDA, 2015). So far, there is no publication regarding the development and validation of Stability Indicating HPLC method for DAPA. This way, it is necessary and extremely important an analytical methodology for this purpose.

Materials and Methods

The chromatographic conditions were as follows: Synergi Fusion C18 column (150 x 4.6 mm) maintained at 30 °C, injection volume of 20 µL, flow rate of 1.0 mL/min, running time of 10 min, mobile phase composed of acetonitrile and water acidified with 0.1% formic acid (42:58, v/v) and detection at 245 nm. Reference sample solution was submitted to forced degradation in acid media, basic, oxidative, heat, and photolytic. Mass identification of degradation products were conducted by UPLC-TOF (Waters).

Results and Discussion

Degradation products and significant reduction of active area could be observed after exposure to UV light and daylight. The excipients did not show any interference in the analysis. The developed method was linear in the range of 1 to 100 µg/mL ($r^2=0.9997$). In repeatability and between-analysts precision studies, DAPA showed RSD values lower than 5%. The method demonstrated to be accurate within the range of interest, showing a mean recovery of 81.66, 100.47 and 119.35%. The limit of detection and quantitation were 0.09 and 0.28 µg/mL, respectively. The method was robust across the randomized variations (p>0.05). The analysis of tablets containing 5 and 10 mg of DAPA resulted in an assay of 99.47 and 101.33%, respectively. A degradation product was found in the forced degradation by UV light. The degradation product showed a molar mass of 817.28 g/mol, which is possibly a dimer of DAPA, since this drug has a molar mass of 408.87 g/mol.

Conclusion

Stress studies revealed that drug was most susceptible to photolytic degradation, revealing one degradation product, whose identification revealed the presence of a possible dimer DAPA. The methodology was validated, and was successfully applied for the quantitative analysis of dapagliflozin in pharmaceutical formulations.

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References

