Application of Quality by Design to optimize a stability-indicating LC method for the determination of ticagrelor and its impurities

Nathalie Wingert, Jéssica B. Ellwanger, Lívia M. Bueno, Caren Gobetti, Cássia V. Garcia, Martin Steppe, Elfrides E.S. Schapoval

PII: S0928-0987(18)30144-1
DOI: doi:10.1016/j.ejps.2018.03.029
Reference: PHASCI 4458

To appear in: *European Journal of Pharmaceutical Sciences*

Received date: 4 December 2017
Revised date: 21 February 2018
Accepted date: 24 March 2018

Please cite this article as: Nathalie Wingert, Jéssica B. Ellwanger, Lívia M. Bueno, Caren Gobetti, Cássia V. Garcia, Martin Steppe, Elfrides E.S. Schapoval , Application of Quality by Design to optimize a stability-indicating LC method for the determination of ticagrelor and its impurities. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Phasci(2017), doi:10.1016/j.ejps.2018.03.029

Application of Quality by Design to optimize a stability-indicating LC method for the determination of ticagrelor and its impurities

Nathalie Wingert [a]*, Jéssica B. Ellwanger [a], Lívia M. Bueno [a], Caren Gobetti [a], Cássia V. Garcia [a], Martin Steppe [a], Elfrides E. S. Schapoval [a]

[a] Laboratory of Pharmaceutical Quality Control – State University of Rio Grande do Sul, Porto Alegre, Brazil.

* Correspondent author: nath.rw@gmail.com, phone: +555133085214

ABSTRACT

Simultaneous analysis of drug compounds and their impurities of degradation and synthesis became constant in the modern pharmaceutical analysis. Likewise, analytical techniques must improve sensitivity and selectivity for the monitoring of pharmaceutical products, allowing a full assessment of impurities in drug products and, therefore, ensure safety and efficacy of pharmacological treatments. The application of Quality by Design (QbD) principles has proved to be feasible on the elaboration of analytical methods, allowing the comprehensive evaluation and measurement of different analytical parameters and their effects on critical properties of the methodology in development. QbD approach was applied to the development of a fast and selective HPLC method for the analysis of the antiplatelet aggregation drug ticagrelor and its degradation products in presence of three impurities of synthesis. Fractional factorial resolution V was the screening experimental design applied to five method parameters. Response surface methodology was carried by central composite star face design on the two critical method parameters selected. Analytical design space, established after the application of Monte-Carlo simulations, verified whether predicted results were in accordance with critical quality attributes. The developed and validated HPLC method with DAD detection at 225 nm was able to resolve eight related compounds in less than three minutes.

Keywords: Quality by Design; Drug impurities; Ticagrelor; HPLC; AQbD