SOCIEDADE PORTUGUESA DE QUÍMICA

ANALÍTICA 2018

9th Meeting of Division of Analytical Chemistry

26-27 MARCH, PORTO-PORTUGAL

FFUP/ICBAS – UNIVERSITY OF PORTO

www.analitica2018.eventos.chemistry.pt

BOOK OF ABSTRACTS

TÍTULO
Book of Abstracts Analítica 2018 - 9th Meeting
of Division of Analytical Chemistry

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EDITION
Sociedade Portuguesa de Química
Av. da República, 45 - 3º Esq
1050-187 Lisboa - Portugal
ISBN: 978-989-8124-21-0

DATE
March 2018

PG 8

SIMULTANEOUS DETERMINATION OF DAPSONE AND CLOFAZIMINE IN NANOFORMULATIONS BY HPLC

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The multidrug therapy with dapsone (DAP) and clofazimine (CLZ) is known as an effective treatment against *Mycobacterium leprae*. However, the low bioavailability and non-specific distribution can reduce therapy efficacy and produce side effects. The use of nanotechnological approaches was explored as a promising carrier for delivery enhancement of these drugs. Therefore, a simple and precise high-performance liquid chromatography (HPLC) method with UV/Vis detection has been developed and validated for the simultaneous determination of DAP and CLZ loaded in solid dispersion and poly(D,L-lactide-co-glycolic acid) nanoparticles, respectively, targeting therapy improvement.

A reversed phase Kinetex core-shell C18 column at room temperature followed by UV/Vis detection at 280 nm was used for chromatographic separation. The elution was performed in gradient mode using aqueous acetate buffer (50 mol L^{-1}, pH 4.8) and an increasing acetonitrile content from 27 to 63% (v/v), at a flow rate of 1.0 mL min^{-1}. The injection volume was fixed at 20 µL and total run time was 23.0 min, with a retention time of 6.0 min for DAP and 14.0 min for CLZ.

The method was validated according to EMA guideline and showed specificity, accuracy (between 99.6 and 114.0% of nominal values) and precision for intra-day (RSD ≤1.8%) and inter-day assays (RSD ≤12.5%). Calibration curves were linear (r^2 >0.9979) and LOD ≤0.03 and LOQ ≤0.06 mg L^{-1} were obtained. Stability was studied after 24 h at room temperature and over three freeze-thaw cycles, and recovery values ≥86.2% were obtained. Precipitation of CLZ was observed at low temperatures (4 °C). Entrapment efficiency in nanoformulations was evaluated as 54.8 ± 0.1% for DAP and 24.9 ± 0.2% for CLZ. The developed method was successfully validated for the simultaneous determination of DAP and CLZ in nanoparticles.

Acknowledgements: This work received financial support from the European Union (FEDER funds) and National Funds (FCT/MEC, Fundação para a Ciência e a Tecnologia and Ministério da Educação e Ciência) under the Partnership Agreement PT2020 UID/QUI/50006/2013 - POCI/01/0145/FEDER/007265. E. M. P. Silva and S. A. C. Lima acknowledge funding from FEDER - Operational Competitiveness and Internationalization Programme (COMPETE 2020) through project NORTE-01-0145-FEDER-000011. L. Barreiros thanks FCT and POCH (Programa Operacional Capital Humano) for her Post-Doc grant (SFRH/BPD/89668/2012). L. L. Chaves thanks the CNPq Foundation, Ministry of Education of Brazil for the Doctoral fellowship 246514/2012-4. Technical assistance from Ms. Manuela Barros is acknowledged.