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Abstract

Box–Behnken Assisted HPLC Development of Simultaneous Determination of Doxorubicin and Vorinostat Encapsulated into Polymeric Nanoparticles †

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The objects of the present study are nanoparticles (NPs) based on a copolymer of lactic and glycolic acids (PLGA), loaded with the anticancer drug doxorubicin (DOX-NP) and histone deacetylase inhibitor vorinostat (SAHA-NP) and developed for breast cancer treatment. Drug encapsulation into the PLGA matrix improves drug safety profiles and allows us to overcome multidrug resistance. In the current study, we developed a high-performance liquid chromatography method for the simultaneous determination of DOX-NP and SAHA-NP using a Box–Behnken design, followed byvalidation and NPs stability determination after sterilization treatment with γ-irradiation.

The separation was performed using a Nucleodur C-18 Gravity column (250 mm × 4.6 mm × 5 µm). Samples were prepared by precipitating PLGA with dimethyl sulfoxide. Three independent variables were analyzed to determine the most optimal conditions: methanol concentration (0–20%), pH (2.5–4.5) and flow rate (0.8–1.2 mL/min). We evaluated the contributions of these variables to the peak resolution and retention time of the last peak of the analyte using a Box–Behnken design. Next, we simultaneously optimized all dependent variables and established their most optimal values using the desirability function.

The optimized method was accurate, precise and linear, in the range of 4.2–52.0 µg/mL for both drugs (R^2 = 0.9999 for vorinostat and R^2 = 0.9988 for doxorubicin). γ-irradiation at a dose of 25 kGy resulted in a degradation of DOX-NP of less than 95%, while the amount of SAHA-NP impurities was 88%.

Thus, the developed method is suitable for simultaneous analysis of DOX-NP and SAHA-NP, including the analysis of impurities.

Supplementary Materials: The presentation material of this work is available online at https://www.mdpi.com/article/10.3390/ECMC2022-13493/s1.

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