Preparation of Deuterium-Labeled Armodafinil by Hydrogen–Deuterium Exchange and Its Application in Quantitative Analysis by LC-MS

Autorzy

Paulina Grocholska

Robert Wieczorek

Remigiusz Bąchor

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Streszczenie

Armodafinil, the R enantiomer of modafinil, was approved in 2007 by the US Food and Drug Administration as a wake-promoting agent for excessive sleepiness treatment. Due to its abuse by students and athletes, there is a need of its quantification. Quantitative analysis by liquid chromatography-mass spectrometry, however, though very common and sensitive, frequently cannot be performed without isotopically labeled standards which usually have to be specially synthesized. Here we reported our investigation on the preparation of deuterated standard of armodafinil based on the simple and inexpensive hydrogen–deuterium exchange reaction at the carbon centers. The obtained results clearly indicate the possibility of introduction of three deuterons into the armodafinil molecule. The introduced deuterons do not undergo back exchange under neutral and acidic conditions. Moreover, the deuterated and non-deuterated armodafinil isotopologues revealed co-elution during the chromatographic analysis. The ability to control the degree of deuteration using different reaction conditions was determined. The proposed method of deuterated armodafinil standard preparation is rapid, cost-efficient and may be successfully used in its quantitative analysis by LC-MS.

Słowa kluczowe

LC-MS, armodafinil, internal standards, hydrogen–deuterium exchange, HDX, isotope dilution

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