DEVELOPMENT OF MIXED-MODE POLYMERIC SORBENT FOR THE DETERMINATION OF MEDICINE DRUG IN BIOLOGICAL MATRICES

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Zopiclone is nonbenzodiazepine hypnotic drug that is used for the treatment of insomnia. This drug was developed with the intent to overcome some disadvantages of benzodiazepines, such as dependence and next day sedation [1,2]. Several analytical methods based on chromatographic and electrophoretic techniques for the determination of zopiclone have been reported [3]. However, it is essential to develop a fast and sensitive method for the determination of zopiclone in the biological matrix.

In order to perform analyte determination in the extract by gas chromatography with negative ion chemical ionization mass spectrometry the selection of solid phase extraction (SPE) sorbent as well as washing and eluting solvents is particularly important. Zopiclone in the sample at the acidic pH has a positive charge, thus cation exchange sorbent such as mixed-mode Oasis MCX could be appropriate. This sorbent is capable to interact with analyte by hydrophilic-lipophilic and ion-exchange interactions [4,5] and therefore it is suitable for achieving an efficient extraction of zopiclone.

The retention and elution of zopiclone could be affected by the pH of the sample solution, which was varied from pH 1 to pH 10. Special attention was paid for to the selection of washing and eluting solvent in the SPE procedure, resulting in very pure and free from moisture extract, which can successfully be applied for gas chromatography-mass spectrometry. Different solvents or mixtures of solvents for elution of the adsorbed analyte, and washing step eliminating interferences in the column were tested.

The acidic solution at pH 4.0 was used during the sample loading step. Column with adsorbed zopiclone (pK_a 6.79 ± 0.42) via ion-exchange interactions, could be washed with a pure organic solvent (1-propanol) in order to remove acidic and neutral interfering compounds. Then analyte was eluted with acetonitrile containing 4 % of NH_4OH. After these steps visibly cleaner extracts were obtained in comparison with those obtained using reversed-phase interactions.

The developed method for zopiclone determination in biological matrices was validated following the recommendation for new methods [6,7,8]. The linear relationships with the correlation coefficients (r^2) better than 0.9960, LOD and LOQ values equal to 0.60 ng mL^{-1} and 2.00 ng mL^{-1} were evaluated. It was determined that extraction efficiency ranged from 82.9 (±6.2) % to 94.6 (±3.4) %. The precision (RSD) for zopiclone was between 4.08 - 9.52 %, while the accuracy was in the range of 93.0 - 106.3 %. The presented method has several advantages over other methods: elimination of interferences and low-volume of samples (0.2 mL). Effective sample preparation as well as relatively short time of analyses proved a great applicability of presented method in clinical laboratories.

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