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Recent advances in analytical techniques for the determination of pregabalin in pharmaceutical and biological samples

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Abstract

Pregabalin (PGB), is an antiepileptic and analgesic drug, which is structural analogue of γ-amino-butyric acid. This drug has been approved by Food and Drug Administration for the treatment of central nervous system disorders including epilepsy, fibromyalgia and also for the treatment of neuropathic pain. It was designed as a potent successor to gabapentin. PGB is minimally metabolized and primarily excreted through urine in an unchanged form. It has predictable pharmacokinetics with excellent bioavailability and has minimal binding to serum proteins. Therefore, determination the content of pregabalin is very important. In this article the studies of detection methods for pregabalin in recent years are reviewed.

Keywords: pregabalin; PGB; determination; detection; sensor.

1. Introduction

Pregabalin (PGB), (S)-3-(amino methyl)-5-methylhexanoic acid, is a novel analogue of the neurotransmitter gamma amino butyric acid with analgesic, anticonvulsant, and anxiolytic activity. It is a white crystalline solid with molecular formula $C_8H_{17}NO_2$, molecular mass of 159.23 g/mol and melting point from 190°C to 192°C [1-3]. It was approved in the year 2007 for adjunctive treatment of partial seizures in adults in United States and Europe, and for the treatment of neuropathic pain from post-therapeutic neuralgia and diabetic neuropathy [4-6]. It was designed as a more potent successor to gabapentin. PGB binds potentially to the α_2-δ subunit, an auxiliary protein, of Q-type voltage-sensitive calcium channels that are widely distributed throughout the peripheral nervous system and central nervous system. There is no official method developed for the analysis of pregabalin till now and therapeutic importance of the drug has engendered development of assays for the quantification of PGB [7-9]. In this paper, the attributes of different analytical technique for the determination of pregabalin in recent years are reviewed.

2. Analytical Methods

2.1. Spectrophotometric method. High sensitivity, sufficient accuracy, simplicity, speed and the necessity of less expensive apparatus make spectrophotometric method as an attractive method for the determination of pregabalin in samples with different matrices such as biological and pharmaceutical samples [10,11].

Onal [12] described three simple, quick and sensitive methods for the spectrophotometric determination of PGB in pharmaceutical preparations. Among them, the first two methods were based on the reaction of PGB as n-electron donors with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and 7,7,8,8-tetracyanoquinodimethane (TCNQ) as π-acceptors to give highly colored complex species. The colored

products were quantitated spectrophotometrically at 494 and 841 nm for DDQ and TCNQ, respectively. Optimization of the different experimental conditions was conducted. Beer's law was obeyed in the concentration ranges 2.0-30.0 and 1.5-10 µg mL^{-1} for DDQ and TCNQ methods, respectively. The third method was based on the interaction of ninhydrin with primary amine present in the pregabalin. This reaction produced a blue colored product in *N*,*N*-dimethylformamide medium, which absorbed maximally at 573 nm. Beer's law was found in the concentration range 40.0-180.0µg mL^{-1}. The methods were applied successfully to the determination of this drug in pharmaceutical dosage forms.

Najam *et al.* [13] developed a simple, reliable, sensitive and accurate spectrophotometric method for the determination of an anticonvulsant drug, PGB. The method was based on the condensation reaction of PGB with p-dimethylaminobenzaldehyde in acid medium. The condensation product showed λ_{max} at 420 nm. They carefully studied and optimized the different parameters affecting the stability of the condensation product. The calibration plots were constructed over the concentration range of 40-120 µg ml^{-1}. The proposed method was successfully applied to the analysis of the drug in dosage form. The high sensitivity of the proposed method allowed the determination of PGB in bulk and in pharmaceutical preparations.

2.2. HPLC method. High-performance liquid chromatography (HPLC) is a powerful tool that enables the separation of complex mixtures into individual components, and is a highly sensitive and reproducible analytical technique. In recent years, HPLC has been combined with many sensitive detection techniques and has experienced continuous improvement of stationary phases, which have improved its sensitivity and specificity. HPLC is currently widely used for the analysis of drugs and dosage forms with respect to quality control, quantitative determination of active ingredients and impurities, monitoring drug blood concentration in patients, and bioequivalence assessment [14,15].

Martinc *et al.* [16] developed a simple analytical method for simultaneous determination of four second generation antiepileptic drugs, including gabapentin, PGB, vigabatrin, and topiramate. Analytes were extracted from human plasma using universal solid phase extraction, derivatized with 4-chloro-7-nitrobenzofurazan (NBD-Cl) and analyzed by HPLC with fluorescence detection. They confirmed that NBD-Cl reacted with sulfamate group of topiramate similarly as with amine group of the other three analytes using mass spectrometry. The method was linear across investigated analytical ranges (0.375–30.0µg/mL for gabapentin, PGB, and vigabatrin; 0.50–20.0µg/mL for topiramate). Intraday and interday precision didn't exceed 9.4%. The accuracy was from 95.6% to 106.0%. The recovery was higher than 80.6%, and the lower limit of quantification was at least 0.5µg/mL. The method was selective and robust. For topiramate determination the method was compared to a previously published method and the results obtained by the two methods were in good agreement. The developed method is suitable for routine therapeutic drug monitoring.

Dzygiel *et al.* [17] developed a sensitive and selective analytical method for the quantification of pregabalin, sildenafil and the active desmethyl metabolite of sildenafil (UK-103320). The method could simultaneously quantify the three analytes within the expected in vivo concentration ranges using 50 µL of rat plasma. It utilized solid-phase extraction followed by HPLC coupled with tandem mass spectrometry. Quantitation in rat plasma demonstrated good accuracy and precision over the following dynamic ranges for each analyte: pregabalin (70–10,000 ng mL^{-1}), sildenafil (1–2,000 ng mL^{-1}) and UK-103320 (1–2,000 ng mL^{-1}). For each analyte, the following lower limits of quantitation were obtained: 70 ng mL^{-1} for pregabalin and 1 ng mL^{-1} for sildenafil and UK-103320, respectively. The method was successfully used to analyze plasma samples from rats when pregabalin and sildenafil were administered in combination.

2.3. Other methods. In addition to these main approaches mentioned above for pregabalin detection, still a few special techniques with high sensitivity have been applied. Wong *et al.* [18] proposed the determination of the effective dose of pregabalin on human experimental pain using the sequential up-down method. Mudiam *et al.* [19] proposed the development, validation and comparison of two microextraction techniques for the rapid and sensitive determination of pregabalin in urine and pharmaceutical formulations after ethyl chloroformate derivatization followed by gas chromatography–mass spectrometric analysis. Rodriguez *et al.* [20] developed a strategy of direct determination of pregabalin in human urine by nonaqueous CE-TOF-MS.

3. Conclusions

Pregabalin is an effective drug used for the treatment of epilepsy, neuropatic pain and anxiety. The wide use of this drug has prompted many researches to develop sensitive and accurate analytical methods for its determination, especially for routine quality control in the analysis of pharmaceutical products [21,22]. This review has highlighted the significant developments in rapid and alternative techniques for the detection of pregabalin in recent years. We believe the development of pregabalin sensors with better sensitivity and specificity, lower cost, simplicity, along with in vivo analytical technique is still the future effort.

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References

[1] Gujral RS, Haque SM, Kumar S. A novel method for the determination of pregabalin in bulk pharmaceutical formulations and human urine samples, African Journal of Pharmacy and Pharmacology 2009; 3(6):327-334.

[2] Dahl SR, Olsen KM, Strand DH. Determination of gamma-hydroxybutyrate (GHB), beta-hydroxybutyrate (BHB), pregabalin, 1,4-butane-diol (1,4BD) and gamma-butyrolactone (GBL) in whole blood and urine samples by UPLC-MSMS, J Chromatogr B 2012; 885:37−42.

[3] Chen XH, Zhang DL, Deng J, Fu XT. Determination of optical impurity of pregabalin by HPLC with pre-column chiral derivatization, J Chromatogr Sci 2008; 46(1): 42-44

[4] Mandal U, Sarkar AK, Gowda KV, Agarwal S, Bose A, Bhaumik U *et al*. Determination of pregabalin in human plasma using LC-MS-MS, Chromatographia 2008; 67(9-4):237-243.

[5] Vaidya VV, Yetal SM, Roy SMN, Gomes NA, Joshi SS. LC-MS-MS determination of pregabalin in human plasma, Chromatographia 2007; 66(11-12):925-928.

[6] Pauly C, Yegles M, Schneider S. Pregabalin determination in hair by ultra-high-performance liquid chromatography tandem mass spectrometry, J Anal Toxicol 2013; 37(9):676-679.

[7] Martinc B, Grabnar I, Mrhar A, Vovk T. Rapid high-performance liquid chromatography method for determination of pregabalin in a pharmaceutical dosage form following derivatization with fluorescamine, J AOAC Int 2010; 93(4):1069–1076.

[8] Chahbouni A, Sinjewel A, den Burger JCG, Vos RM, Wilhelm AJ, Veldkamp AI *et al*. Rapid quantification of gabapentin, pregabalin, and vigabatrin in human serum by ultraperformance liquid chromatography with mass-spectrometric detection, Ther Drug Monit 2013; 35(1): 48–53.

[9] Vermeij TAC, Edelbroek PM. Simultaneous high-performance liquid chromatographic analysis of pregabalin, gabapentin and vigabatrin in human serum by precolumn derivatization with o-phtaldialdehyde and fluorescence detection, J Chromatogr B 2004; 810(2):297–303.

[10] Bali A, Gaur P. A novel method for spectrophotometric determination of pregabalin in pure form and in capsules, Chem Cent J 2011; 5:59.

[11] Onal A, Sagirli O. Spectrophotometric and spectrofluorimetric methods for the determination of pregabalin in bulk and pharmaceutical preparation, Spectroc Acta Pt A-Molec Biomolec Spectr 2009; 72(14):68-71.

[12] Armagan O. Development and validation of selective spectrophotometric methods for the determination of pregabalin in pharmaceutical preparation, Chin J Chem 2009; 27(4):781-786.

[13] Najam R, Shah GM, Andrabi SMA. Kinetic spectrophotometric determination of an important pharmaceutical compound, pregabalin, J Anal Sci Technol 2013; 4:22.

[14] Kasawar GB, Farooqui MN. Development and validation of HPLC method for the determination of pregabalin in capsules, Indian J Pharm Sci 2010; 72(4):517–519.

[15] Souri E, Eskandari M, Tehrani MB, Adib N, Ahmadkhaniha R. HPLC determination of pregabalin in bulk and pharmaceutical dosage forms after derivatization with 1-fluoro-2,4-dinitrobenzene, Asian J Chem 2013; 25(13):7332–7336.

[16] Martinc B, Roskar R, Grabnar I, Vovk T. Simultaneous determination of gabapentin, pregabalin, vigabatrin, and topiramate in plasma by HPLC with fluorescence detection, J Chromatogr B 2014; 962:82-88.

[17] Dzygiel P, Fraier D. Simultaneous determination of pregabalin, sildenafil and its active metabolite in rat plasma utilising SPE followed by LC-MS-MS, Chromatographia 2011; 73(11-12):1177–1182.

[18] Wong W, Wallace MS. Determination of the effective dose of pregabalin on human experimental pain using the sequential up-down method, J Pain 2014; 15(1):25–31.

[19] Mudiam MKR, Chauhan A, Jain R, Ch R, Fatima G, Malhotra E *et al*. Development, validation and comparison of two microextraction techniques for the rapid and sensitive determination of pregabalin in urine and pharmaceutical formulations after ethyl chloroformate derivatization followed by gas chromatography-mass spectrometric analysis, J Pharm Biomed Anal 2012; 70:310–319.

[20] Rodriguez J, Castaneda G, Munoz L. Direct determination of pregabalin in human urine by nonaqueous CE-TOF-MS, Electrophoresis 2013; 34(9-10):1429–1436.

[21] Walash MI, Belal F, El-Enany N, El-Maghrabey MH. Simple and sensitive spectrofluorimetric method for the determination of pregabalin in capsules through derivatization with fluorescamine, Luminescence 2011; 26(5):342-348.
[22] Kostic N, Dotsikas Y, Malenovic A. Critical review on the analytical methods for the determination of zwitterionic antiepileptic drugs-vigabatrin, pregabalin, and gabapentin-in bulk and formulations, Instrum Sci Technol 2014; 42(4):486-512.

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