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Research Article

APPLICATION OF ION PAIR EXTRACTIVE SPECTROPHOTOMETRIC METHODS FOR THE DETERMINATION OF GABAPENTIN IN PHARMACEUTICAL FORMULATION

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ABSTRACT

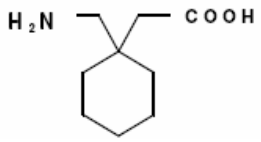
Two new simple, selective, sensitive and economical methods (A and B) have been developed for the analysis of gabapentin in pure and dosage form. The methods were based on ion-pair complexation between drug and dyes like metanil yellow and thymol blue at an optimum pH of 2.8. The colored chromogens were measured at 410 nm (λmax) for method A and 550 nm (λmax) for method B. Calibration curve was linear in the range of 0.2 - 2.0 µg/ml for method A and 0.1 - 1 µg/ml for method B. Different analytical performance parameters such as linearity, precision and accuracy were determined. The proposed methods were validated and successfully applied for analysis of bulk and tablet dosage forms.

Keywords: Gabapentin, Metanil yellow, Thymol blue, Ion pair chromatography, Validation.

INTRODUCTION

Gabapentin [1-(Amino methyl) cyclohexane acetic acid] is a novel antiepileptic agent, originally developed as a gamma-amino butyric acid (GABA) mimetic compound to treat spasticity and has been shown to have potent anticonvulsive effects. Gabapentin acts by irreversible inhibition of gaba transaminase enzyme, thus preventing the degradation of gaba in brain. Gabapentin is well absorbed from gastrointestinal tract after 2 hours of oral dosage and peak plasma concentration is achieved [1].

The literature survey revealed few analytical works for determination of gabapentin in formulations. These include colorimetry [2, 3], UV-spectroscopy [4, 5], HPTLC [6, 7], HPLC [8, 9], and other hyphenated techniques [10, 11]. The present study aims to develop two simple, specific, accurate, precise, economical methods for determination of gabapentin. These methods are based on the reaction of drug, in its protonated state with anionic species (acidic dyes) to form ion pair complex, and can be extracted by organic solvents such as chloroform, dichloromethane and benzene. The colored complex produced can be measured spectrophotometrically at 410 and 550 nm. Here metanil yellow (method A) and thymol blue (method B) were used.



Gabapentin

MATERIALS AND METHODS

A Shimadzu model UV-1700 double beam UV-Visible spectrophotometer with a pair of 1 cm matched quartz cells was used. Gabapentin was gifted by Micro Labs, Bangalore, India. The commercial tablets of gabapentin was procured from a local pharmacy. All the other reagents used were of analytical grade.

Preparation of standard solutions

A stock solution was prepared by dissolving 50 mg of gabapentin in 50 ml chloroform to obtain a concentration of 1000 µg/ml. Various aliquots of stock solution of gabapentin were suitably diluted with

chloroform to get concentrations in the range of 0.2-2 µg/ml for method A and 0.1-1 µg/ml for method B.

Method development

Ten milliliters of these solutions were added into different separating funnels, into which 2 ml of buffer solution (pH 2.8) and 2 ml of dye solution-metanil yellow (0.1%, w/v) for method A and thymol blue (0.05%, w/v) for method B were added. The yellow color developed was measured at 410 nm for method A and the blue color developed was measured at 550 nm for method B. The linearity of gabapentin with ion pair reagents were constructed.

Optimization of parameters

The optimum dye concentration, dye volume, pH and buffer capacities were selected on the basis of their ability to give maximum absorbance, as shown in Table-1

Table 1: Optimization of parameters

Method	Dye concentration	Dye volume	pH	Buffer capacity
Method A (Metanil Yellow)	0.1 % w/v	2 ml	2.8	2 ml
Method B (Thymol blue)	0.05 % w/v	2 ml	2.8	2 ml

Preparation of sample solution and formulation analysis

Twenty tablets were weighed and average weight of each tablet was determined. The tablets were powdered and weight equivalent to 50 mg was accurately weighed and was transfer to 50 ml volumetric flask and extracted with chloroform. The resulting solution was filtered through Whatmann filter paper and the filtrate was suitably diluted with chloroform to give a concentration of 1 µg/ml of gabapentin for method A and 0.5 µg/ml for method B. The solutions were transferred to two separating funnels. It was followed by the addition of 2 ml of buffer solution (pH 2.8) and 2 ml of dye solutions. The absorbance of these solutions were measured at 410 nm for method A and 550 nm for method B respectively. The procedure was repeated five times for each brand.

Validation of the proposed method

The proposed method was validated according to the International Conference on Harmonization (ICH) guidelines [12] and following parameters were evaluated.

The accuracy of the methods were checked by recovery studies. To the pre analyzed solution of sample a known quantity of standard drug was added and mixed well and proceeded as assay. Precision of the methods were studied by inter-day and intra-day analysis of multiple samplings of homogenous sample and expressed as % RSD. The limit of detection and quantification (LOD and LOQ) was calculated using the following equation as per ICH guidelines. LOD = 3.3 × σ/S, LOQ = 10 × σ/S., where σ is the standard deviation of the response and S is slope of calibration curve.

Table 2: Validation parameters of gabapentin

Parameters		Method A	Method B
Absorption maxima (nm)		410	550
Linearity range (µg/ml)		0.2-2.0 µg/ml	0.1-1.0 µg/ml
Regression equation	Slope	0.474	0.871
	Intercept	0.089	0.054
Regression coefficient (r^2)		0.992	0.994
Sandell's sensitivity (µg/cm^2/0.001A.U)		0.00178	0.00137
Limit of Detection (µg/ml)		0.09	0.04
Limit of Quantification.(µg/ml)		0.18	0.08
[a]Precision	Repeatability (% RSD)	0.56	0.73
	Inter-day (% RSD)	0.84	0.68
	Intra-day (% RSD)	0.65	0.98
	Analyst (% RSD)	0.73	1.03
[b]Formulation analysis	Brand I (% label claim)	99.78	100.02
	Brand II (% label claim)	101.07	99.69

[a]Average of three determinations, [b]Average of five determinations.

RESULTS AND DISCUSSION

The developed method was validated as per ICH guidelines for linearity, precision and recovery studies. The accuracy of the method was proved by performing recovery studies in the commercially available formulation. The precision of the method were checked in terms of intra-day and inter-day conditions and the result were satisfactory. The analysis of results showed that the presence of excipients do not interfere with the final determination of the drug. The amount of gabapentin found in the assay was agreed with label claim.

Table 3: Data for recovery studies

Method	Amount added (mg)	Amount recovered* (mg)	Recovery (%)	% RSD
Method A	5	4.95	99.02	0.28
	10	9.98	99.80	
	15	14.98	99.86	
Method B	5	4.98	99.60	0.26
	10	9.90	99.01	
	15	14.96	99.73	

*Average of three determinations

CONCLUSION

The validated ion pair spectrophotometric methods employed here proved to be simple, fast, accurate, precise and sensitive. The proposed methods can be applied for routine analysis in quality control laboratories.

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