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Development and validation of sensitive spectrophotometric method for determination of two antiepileptics in pharmaceutical formulations

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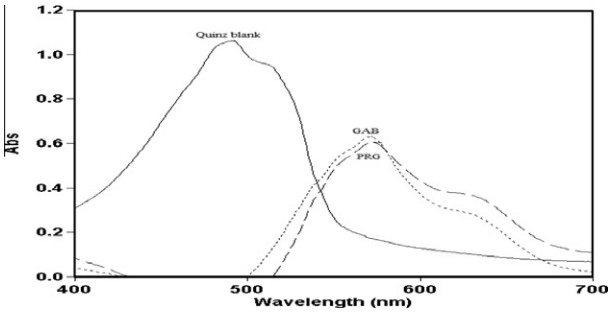
HIGHLIGHTS

- We validated novel and sensitive spectrophotometric method for determination of two antiepileptics.
- The method involves the formation of charge transfer complex between drugs and quinalizarin or alizarin red S.
- Beer's law is obeyed in the concentration ranges 0.4–10 μg mL^{-1}.
- The formed complexes were very stable.

GRAPHICAL ABSTRACT



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ABSTRACT

Rapid, sensitive and validated spectrophotometric methods for the determination of two antiepileptics (gabapentin (GAB) and pregabalin (PRG)) in pure forms and in pharmaceutical formulations was developed. The method is based on the formation of charge transfer complex between drug and the chromogenic reagents quinalizarin (Quinz) and alizarin red S (ARS) producing charge transfer complexes in methanolic medium which showed an absorption maximum at 571 and 528 nm for GAB and 572 and 538 nm for PRG using Quinz and ARS, respectively. The optimization of the reaction conditions such as the type of solvent, reagent concentration and reaction time were investigated. Beer's law is obeyed in the concentration ranges 0.4–8.0 and 0.5–10 μg mL^{-1} for GAB and PRG using Quinz and ARS, respectively. The molar absorptivity, Sandell sensitivity, detection and quantification limits are also calculated. The correlation coefficients were $\geqslant$0.9992 with a relative standard deviation (RSD%) of $\leqslant$1.76. The methods are successfully applied to the determination of GAB and PRG in pharmaceutical formulations and the validity assesses by applying the standard addition technique, which compared with those obtained using the reported methods.

Introduction

Gabapentin (1-(aminomethyl)cyclohexaneacetic acid) (GAB) and pregabalin (PRG), (*S*)-3-aminomethyl-5-methylhexanoic acid (Scheme 1). They are anticonvulsant drugs used in the treatment of epilepsy and neuropathic pain, as an adjunct therapy for partial seizures [1]. Recently, it has been approved for treatment of generalized anxiety disorders in Europe [2,3]. Recently, pregabalin has been approved by the FDA for the treatment of spinal cord injury and as the first drug indicated for the treatment of fibromyalgia. The USP 30 described a liquid chromatographic method for determination of GAB [4]. Pregabalin is not yet the subject of monograph in any pharmacopeia.

Literature survey reveals that there are several methods for the determination of GAB using High performance liquid chromatography

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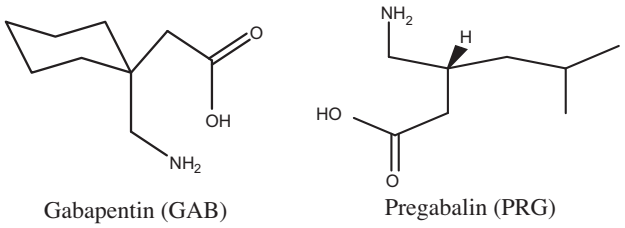

Scheme 1. The chemical structures of the studied drugs and reagents.

(HPLC) [5–12], LCMS [13], capillary electrophoresis [14,15], chemiluminometry [16], potentiometry and titrimetry [17], voltammetry [18,19], spectrofluorimetry [20,21], spectrophotometry [22–32] and automated spectrophotometry using piezoelectric pumping [33] have been employed for determining GAB in pharmaceutical preparations.

Literature survey reveals that the methods adapted to the analysis of PRG in its dosage forms and biological matrices include high-performance liquid chromatography [34–38], with fluorescence detection [39–41], LC-MS-MS [42–45]; spectrofluorimetry [46–50]. These methods require long and tedious pre-treatment of the samples and laborious clean up procedures prior to analysis. An official monograph of PRG does not exist in any pharmacopoeia and determination of PRG in bulk and pharmaceutical formulations has not been yet described. A through literature search has revealed that only few spectrophotometric methods [46,50–59] available for determination of PRG in bulk drug and pharmaceutical formulations. So there is a lot of scope for development of simple and suitable analytical spectrophotometric method for the determination of PRG in bulk and pharmaceutical formulations. UV–VIS spectrophotometry is the technique of choice in research laboratories, hospitals and pharmaceutical industries due to its low cost and inherent simplicity.

However, many of the above methods suffered from one or other disadvantage like poor sensitivity, require high cost solvents in addition to elaborate treatment, need tedious extraction procedures, measurements done at shorter wavelengths, heating or cooling step, use of expensive chemical and/or complicated experimental set-up as can be seen from Tables 1 and 2.

In the present work, we report a very simple, rapid, accurate, and sensitive visible spectrophotometric method to assay GAB and PRG in pure forms and in pharmaceutical formulations (capsules). The proposed methods involves the formation of charge transfer complex between drugs and alizarin derivatives; quinalizarin (Quinz) and alizarin red S (ARS) as chromogenic reagents. The main advantages of the proposed methods are being simple, rapid and not require tedious extraction procedure. Compared to other reported spectrophotometric methods, the proposed methods are either more sensitive or even having comparable sensitivity.

Experimental

Apparatus

All the absorption spectral measurements were made using Varian double beam UV–VIS spectrophotometer (Tokyo, Japan) equipped with 10 mm matched quartz cells.

Table 1
Comparison between the reported spectrophotometric methods for determination of GAB.

	Reagent/s used	λ_{max} (nm)	Concentration range ($\mu g\ mL^{-1}$)	Molar absorptivity ($L\ mol^{-1}\ cm^{-1}$)	LOD ($\mu g\ mL^{-1}$)	Remarks	Refs.
1.	UV-spectrophotometry	210	0.25–3.5	–	0.044	Shorter wavelength	[22]
2.	Ninhydrin	405	50–300			Heating required, less sensitive	[23]
3.	Ninhydrin/sodium molybdate mixture	570	0.25–4.8	2.54×10^4	0.059		[24]
4.	a. Iodine	360	6–30	6.19×10^3	0.39	Shorter wavelength	[25]
	b. 7,7,8,8-Tetracyanoquinodimethane (TCNQ)	842	8–24	7.22×10^3	0.48	Less sensitive, use of expensive organic solvent	
	c. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)	456	12–36	9.34×10^3	1.20		
	d. 2,5-Dichloro-3,6-dihydroxy-1,4-benzoquinone (chloranilic acid, pCA)	535	60–200	7.19×10^3	7.59		
	e. Tetracyanoethylene (TCNE)	412	40–140	1.10×10^3	3.54		
	f. 2,3,5,6-Tetrachloro-1,4-benzoquinone (chloranil)	521	40–120	1.23×10^3	3.33		
5.	a. Ninhydrin	568	2.0–30	1.25×10^4	0.15	Heating required, long time	[26]
	b. 2,3,5,6-Tetrachloro-1,4-benzoquinone, (chloranil)	230	16–70	6.1578×10^4	0.44	Less sensitive, use of expensive organic solvent, long time	
	c. Tetracyanoethylene (TCNE)	335	6.0–30	1.0643×10^4	0.2		
	d. 7,7,8,8-Tetracyanoquino-dimethane (TCNQ)	439	4.0–30	6.7743×10^4	0.04		
	e. Chloranilic acid	314	6.0–30	5.7399×10^4	0.09		
	f. 2,3-Dichloro-5,6-dicyano-1,4-benzo-quinone (DDQ)	304	2.0–40	8.7452×10^4	0.08		
6.	1,2-Naphthoquinone-4-sulfonate (NQS)	495	7.5–75	2.06×10^3	2.46	Less sensitive, time consuming	[27]
7.	a. Cupric chloride	246	40–95	1.33×10^3	1.179	Less sensitive, Extraction in organic solvent	[28]
	b. Bromothymol blue	411	100–800	1.99×10^2	1.44		
	c. Bromocresol green	411	10–150	1.54×10^3	1.61		
8.	a. Vanillin (Duquenois reagent)	376	80–360	4.57×10^2		less sensitive measurements at shorter wavelengths, heating required	[29]
	b. Ninhydrin	569	40–280	5.16×10^2			
	c. p-Benzoquinone	369	80–320	4.63×10^2			
9.	Acetylacetone and formaldehyde	415	20–140	1.66×10^3		Heating required, less sensitive	[30]
10.	a. 2,4,6-Trinitrophenol (picric acid)	415	1.25–15.0	1.09×10^4	0.23	Time consuming, expensive organic solvent	[31]
	b. 2,4-Dinitrophenol (2,4-DNP)	420	2.0–18.0	0.64×10^4	0.75		
11.	a. Bromocresol green	416	10–120	1627.70	2.90	Extraction in organic solvent	[32]
	b. Bromothymol blue	421	40–90	1123.72	10.86		
12.	a. Quinalizarin (Quinz)	571	0.4–7.2	1.5743×10^4	0.092		Proposed methods
	b. Alizarin red S (ARS)	528	0.5–10	1.5238×10^4	0.105		