World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

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A concise review on analytical profile of Vigabatrin

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World Journal of Advanced Research and Reviews, 2023, 17(02), 061–067

Publication history: Received on 19 December 2022; revised on 29 January 2023; accepted on 01 February 2023

Article DOI: https://doi.org/10.30574/wjarr.2023.17.2.0178

Abstract

Vigabatrin (VGB) is a drug of Anticonvulsant class. It works by decreasing abnormal electrical activity in the brain. It inhibits the GABA-degrading enzyme i.e. GABA transaminase, it increases the GABA concentrations in the brain. Vigabatrin is used for the treatment of refractory complex partial seizures in adults and also used for children 2 years of age and older and infantile spasms in children. Vigabatrin was approved for anticonvulsant medication by USFDA on August 21, 2009. Therefore, in the present review article, we have enlisted different analytical method such as Ultraviolet (UV) visible spectroscopy, High-performance liquid chromatography (HPLC), Ultra-performance liquid chromatography (UPLC) and Gas Chromatography for both qualitative and quantitative analysis of VGB in pharmaceutical and biological. In the future, this review article will assist researchers regarding the development of a new analytical method for VGB.

Keywords: Vigabatrin; Anticonvulsant; USFDA; Analytical Method; HPLC; Bioanalytical Method

1. Introduction

Vigabatrin (VGB) is a new antiepileptic drug (g-vinyl-g-amino butyric acid). It is a structural analogue of the Gama amino butyric acid (GABA) which is inhibitory neurotransmitter. It irreversibly inhibits the action of GABA transaminase; it is an enzyme that degrades the GABA [1]. VGB mostly given in resistant partial and secondarily generalized seizures as add-on therapies, which are not satisfactorily controlled by other antiepileptic drugs [2]. In treatment of refractory partial seizures until the discovery vigabatrin was widely used as adjunctive, in 1997 the severe irreversible visual field constriction associated with its chronic use. Now a days, vigabatrin is rarely used to treat partial seizures, but it is regarded by many authorities as a drug of choice in infants with infantile spasms (West syndrome), mainly tuberous sclerosis cases [3]. The brand name of vigabatrin is sabril and its chemical formula is C6H11NO2. Its chemical name is (RS)-4-aminohex-5-enoic acid [4]. Figure 1. Depicts the chemical structure of VGB.

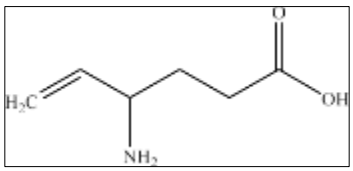

Figure 1 Chemical Structure of Vigabatrin

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1.1. Mechanism of action

Gamma-aminobutyric acid (GABA) is a inhibitory neurotransmitter in the central nervous system. The enzyme responsible for metabolism of vigabatrin in gamma-aminobutyric acid transaminase (GABA-T). VGB increase concentrations of GABA in the central nervous system by irreversibly inhibiting the gamma- aminobutyric acid transaminase (GABA-T) enzyme. VGB is a structural analog of gamma-aminobutyric acid (GABA). Although the vigabatrin exact mechanism of antiseizure effect is unknown, it is thought correlated to the drug's action as a preferential and irreversible inhibitor of GABA transaminase (GABA- T), which degrades the GABA that results the increase in GABA concentrations in the CNS. Vigabatrin have racemic mixture of 2 enantiomers; the pharmacologically active enantiomer is the S enantiomers and the R enantiomer is inactive [5].

1.2. Pharmacokinetics

1.2.1. Absorption

Oral administration of vigabatrin following the essentially complete absorption. The Tmax is approximately 2.5 hours in infants (5months - 2years) and in all other age groups is 1 hour [6].

1.2.2. Distribution

Vigabatrin is widely distributed throughout the body. The mean steady-state volume of distribution of vigabatrin is 1.1 L/kg. It does not bind to plasma proteins [6].

1.2.3. Metabolism

Vigabatrin is not significantly metabolized [6].

1.2.4. Elimination

The vigabatrin is eliminated through urine is approximately 95% of the drug within 72 hours of administration, of which approx. 80% of drug is unchanged parent drug [5].

1.3. Pharmacodynamics

Vigabatrin is used as an antiepileptic agent which is chemically unrelated to other anticonvulsants. VGB prevents the metabolism of GABA by irreversibly inhibiting GABA transaminase (GABA-T). As vigabatrin is an irreversible inhibitor of gamma-aminobutyric acid transaminase (GABA-T), the duration of effect of vigabatrin is thought to be dependent on the rate of GABA-T re-synthesis rather than on the rate of drug elimination [6].

2. Analytical Account of VGB

For the determination of VGB in bulk and pharmaceutical formulations, an exhaustive literature search found numerous analytical techniques such as UV/Visible Spectrophotometry, HPLC, UPLC, Gas Chromatography and bioanalytical approaches. VGB is measured as a single constituent and in combination with Gabapentin (GBP), Pregabalin (PGB) and Topiramate (TOP) in various dosage forms. Figure 2 shows different analytical methods implemented for the estimation of VGB.

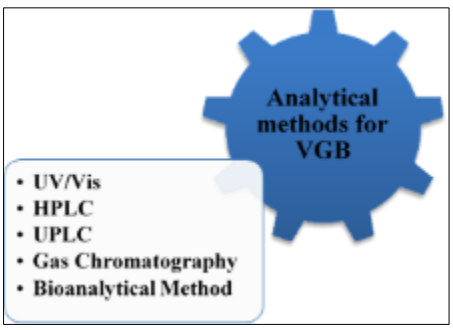

Figure 2 Analytical methods of VGB

2.1. Bio-analytical method for VGB

Bio-analysis is a sub-discipline of analytical chemistry covering the quantitative measurement of xenobiotic (drugs and their metabolites, and biological molecules in unnatural locations or concentrations) and biotics (macromolecules, proteins, DNA, large molecule drugs, metabolites) in biological systems [7]. The summary of the reported bioanalytical methods is shown in Table 1.

Table 1 Bioanalytical determination of VGB

Sr. No.	Drug	Sample Matrix	Method	Column	Detection	Internal Standard	Ref
1	VGB	Human plasma and urine	HPLC	Silica column	460 nm	Aspartam	8
2	VGB	Human plasma and urine	HPLC	C_{18} column	448 nm	Tranexamic acid	9
3	VGB	Human plasma	HPLC	Reversed-phasecellulose-based chiral column	340 nm	1-aminomethyl-cycloheptyl -acetic acid	10
4	VGB	Human serum	HPLC	Spherisorb 3ODS2column	330 nm	L-Homoarginine	11
5	VGB	Human plasma	UPLC	Phenomenex EVOC-18 column	***	[13C, 2H5]-Rac- Vigabatrin	12
6	PGB, GBP, VGB	Human serum	HPLC	Alltima 3C18column	330 nm	Norvaline	13
7	GBP, PGB, VGB, and TOP	Human plasma	HPLC	ZORBAX EclipsePlus C_{18} column	530 nm	p-fluoro-DL-phenylalanine	14
8	GBP, VGB, TOP	Human plasma	HPLC-F	Hydro-RP column	500 nm	Isoniazid	15
9	GBP, VGB	Serum and urine	HPLC	Superspher 60 RP	455 nm	g-phenylGABA	16
10	VGB, GBP	Human serum	GC-MS	Polydimethylsiloxane	***	Cyclobarbital	17
11	VGB, GBP	spiked human plasma	Spectrofluorimetric	***	465 nm	***	18
12	VGB andGBP	Human Urine	Spectrofluorimetric	***	472 nm	***	19

***Not provided

2.1. UV-Visible spectroscopy method for VGB

The spectrophotometric methods have been accounted for the determination of VGB. The details of Spectrophotometry determination of basic principle, sample matrix, lambda max, solvent, linearity range and the correlation coefficient are summarized in Table 2.

Table 2 Spectrophotometric methods used for determination of VGB

Sr. No.	Drug	Matrix	Solvent	Lambda Max (nm)	Linearity (µg/mL)	Correlation coefficient (R2)	Ref.
1	VGB	Dosage forms	5 mM sodium phosphate buffer containing 5 mM benzyl tri-ethylammonium hydroxide (BTEA) at pH 2.2	214 nm.	5-150 µg/ml	0.9911	20
2	VGB	Tablets	ethyl acetate	460 nm	2–10µg/ml	0.9999	21

2.2. HPLC method for VGB

The specificity of the HPLC method is excellent and simultaneously sufficient precision is also attainable. However, it has to be stated that the astonishing specificity, precision, and accuracy are attainable only if wide-ranging system suitability tests are carried before the HPLC analysis. For this reason, the expense to be paid for the high specificity, precision, and accuracy is also high [22]. The summary of the reported HPLC methods is shown in Table 3.

Table 3 Summary of HPLC methods for the determination of VGB in a single and combined dosage form

Sr. No.	Drug name	Column	Mobile phase	Lambda max(nm)	Linearity (µg/mL)	Retention time (min)	Flow rate (mL/min)	Detector	Ref.
1	VGB	C18 Column	10mM Phosphoricacid-acetic acid(75:25)	451 nm	0.0576 - 2.16 µg/20µL	8.1 min	1 ml/min	UV	23
2	VGB	Finpak SIL C18	acetonitrile: water (97.5 : 2.5% V/V)	265 nm	5-30 µg/mL	3.89 min	1 mL/min	UV	24
3	VGB	chirobiotic TAG	ethanol–water(80:20,v/v),	210 nm	100–1600 µg/ml	***	0.4 ml/min	UV	25
4	VGB	Octadecylsilica (ODS)	A - 0.05% (v/v) HCO_2H in [H_2O–MeOH (90:10, v/v)] B - 0.05% (v/v) HCO_2H in [H_2O–MeOH (10:90, v/v)]	333 nm	***	A - 35.41 B – 54.90	0.5 ml/min	Fluorescence	26
	VGB and GBP	5 micro ASMT BANsil CN column	Acetonitrile-TBAH (20 : 80) containing phosphoric acid	390 nm	0.2–1.0 mg/mL	2.94 and 2.92	1mL/min	fluorescence detector	27

***Not provided

2.3. UPLC methods for VGB

The introduction of UPLC often faster analytical separation procedures without sacrificing the high quality result [28]. Many laboratory specialists assured that the UPLC can eventually replace all current HPLC methods. In addition, it is an advanced technology that combines the unique characteristics and outperformances HPLC in several aspects, including greater chromatographic resolution, more sensitive analysis, less time consumption [29-33], reduced solvent use and fast analytical speed [34-36]. Jing Zhao et. al. established UPLC method development and validation for analysis of enantiomeric vigabatrin by derivatization with diacetyl-L-tartaric anhydride. UPLC was carried out in Agilent ZORBAX Rapid Resolution High Definition Eclipse Plus C18 column (100 mm × 2.1 mm, 1.8 µm), by using mobile phase 10 mM ammonium formate (pH 3.0) and methanol at a flow rate of 0.2 mL/min. The linearity of the calibration curve ranged from 0.25-100.0 mg/mL and the regression coefficient (r2) was 0.9987 [37].

Abbreviations

- VGB - Vigabatrin
- USFDA - United states food and drug administration
- UV/VIS - Ultra violet/visible spectroscopy
- HPLC - High-performance liquid chromatography
- UPLC - Ultra performance liquid chromatography
- GC - Gas Chromatography
- RP - Reverse phase
- nm - Nanometer
- µg/mL - Micro gram per Milliliter
- GBP - Gabapentin
- PGB - Pregabalin
- TOP - Topiramate

3. Conclusion

The present review article provides comprehensive data of various analytical and bioanalytical methods developed for VGB alone and in combinations. For analysis purpose, different analytical methods have been reported that includes HPLC, UPLC, UV spectroscopy and gas chromatography, etc. The method along with their details concerning the mobile phase, stationary phase, retention time, etc., have been summarized in tabular form that will more helpful for the researchers for further analytical method development for estimation of VGB in dosage form and pure form. In the future, enlisted data can be used for the development of analytical methods bio-analysis of VGB in pharmaceutical and biological formulations. Finally, it presents an opportunity for greater information on what has already been done and what new methods and changes can be developed to get a better estimation of VGB.

Compliance with ethical standards

Acknowledgments

Authors are thankful to Smt. Sharadchandrika Suresh Patil College of Pharmacy Chopda, Maharashtra, India for providing necessary library facilities.

Disclosure of conflict of interest

The authors declare that no conflict of interest

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