AN ANALYTICAL OVERVIEW OF VOGLIBOSE: A REVIEW

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Abstract

Voglibose is a potent α-glucosidase inhibitor having anti-obesity and anti-diabetic activity used in the treatment of hyperglycemia & type II diabetes mellitus. Much of research work has been done on Voglibose regarding the synthesis, pharmacology, mechanism of actions and in the present article, the authors have focused on various analytical techniques used for the estimation of Voglibose in pharmaceutical formulations. This review covers all the analytical techniques like UV-Visible spectroscopy, HPLC, UPLC and LC-MS for the analysis of Voglibose either as a single or multicomponent dosage form.

Keywords: Voglibose; UV-Visible; LC-MS; HPLC; UPLC; Diabetes Mellitus

INTRODUCTION

Voglibose (code number: AO-128, trade name: Basen®) (1S)-[1(OH),2,4,5/3]-5- {[2-hydroxy-1-(hydroxymethyl) ethyl] amino}-1-*C*-(hydroxymethyl)-1,2,3,4-cyclohexanetetrol], is an *N*-substituted derivative of valiolamine, which is a branched-chain aminocyclitol, or pseudo-amino sugar, and its *N*-substituted moiety is derived from glycerol.[1] Voglibose is generally administered through an oral route. Voglibose (Fig.**2**) has a molecular formula $C_{10}H_{21}NO_7$ and a molecular weight 267.28 g/mole, and it is a white to yellowish white crystalline powder with a metallic taste. Voglibose is soluble in water, chloroform, methanol, ethanol and slightly soluble in 0.1 N NaOH. Voglibose was discovered in 1981 and first commercially released in Japan in 1994.[2] A study has been published in the Journal of Clinical Endocrinology and Metabolism by *Bristol-Myers Squibb*, which is being developed by the company under the trade name BASEN, to improve postprandial hyperglycemia in type II diabetes mellitus.[3] Diabetes Mellitus is a chronic metabolic disorder affecting people worldwide, with significant morbidity and mortality caused by its micro-vascular and macro-vascular complications, affecting various vital organs and structures in humans.[3] The drug's action is due to a reversible inhibition of membrane bound

intestines, where glycosidase hydrolize enzymes hydrolyze oligosaccharides and disaccharides to glucose and other monosacscharides. The pKa value of Voglibose is found to be 7.66. Voglibose is available as tablet with brand name Advog (Enzo Biopharma), Asvogli (A S Pharmaceutical Pvt), Bogli (Sarian Healthcare), Bose (Three Dots Lifescience), PPG (AHPL), Prandial (Cipla Limited) etc. with label claim 0.2, 0.3 mg in India. Voglibose is available in combination with Metformin, Glimepiride, Pioglitazon and Lindagliptin.

Pharmacokinetic parameters are [4]

- ✓ **Absorption:** After oral administration, Voglibose is poorly absorbed. However, Systematic unintended aspects have been observed.
- ✓ **Metabolism:** As a result, liver metabolism of Voglibose is negligible.
- ✓ **Excretion:** There is no renal excretion and no detectable plasma concentrations after oral administration.
- ✓ **Half-life:** 4.08 hours

Usage

- ✓ A dose of 0.2 mg tid before meals are beneficial in NIDDM patients and is recommended. Voglibose should be used in conjunction with diet or diet plus oral hypoglycemic drugs, and dose titration should be recommended only if a response to 0.2 mg tid of voglibose is not seen.
- ✓ Glycemic control was associated with changes in VAT but not SATC, and the higher dose (0.3 mg three times daily) is effective in reducing the reactivity of visceral adipose tissue to Subcutaneous Adipose Tissue.[2]

Side effects are [2]

Soft stools or diarrhea,flatulence, bloating, abdominal fullness, abdominal pain or discomfort, hepatitis with severe cholestasis, Metabolic hypoglycemicpisodes, nausea, vomiting, dizziness.

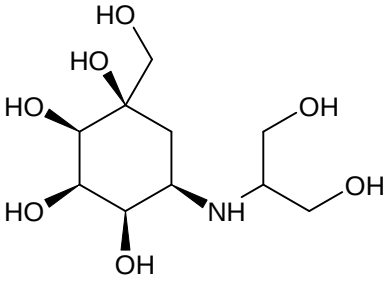

Fig1

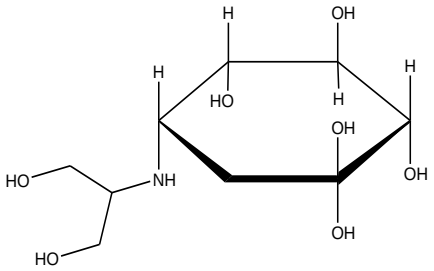

Fig2

In the present study, we have reviewed exclusively the analytical methods developed for the quantification of voglibose in biological samples and pharmaceutical dosage forms. The present review article summarizes the analytical techniques so far developed, such as Spectrophotometry, High-Performance Liquid Chromatography, Ultra Performance Liquid

Chromatography and Hyphenated techniques for the determination of Voglibose and some of the analytical parameters were highlighted.

1. SPECTROPHOTOMETRIC METHOD

Table 1: **Comparative table for Voglibose (VGB) by using Spectrophotometric**

Solvent	λ_{max}	Linearity (µg/ml)	LOD(µg/ml)	LOQ(µg/ml)	Ref.
Methanol (Taurine and Sodium periodate)	282nm	10 -80	–	–	[5]
Water (Taurine and Sodium periodate)	222 nm	0.003 - 0.024	0.00263,	0.0079	[6]
	235 nm (First order derivative spectroscopy)		0.00114	0.0034	
	217 nm - 227 nm (AUC)		0.00272	0.0082	

Table 2: **Comparative table for Voglibose (VGB) in combination by using Spectrophotometric**

Solvent	λ_{max}		Linearity(µg/ml)		LOD (µg/ml)		LOQ (µg/ml)		Ref.
	MET	VGB	VGB	MET	VGB	MET	VGB	MET	
Methanol (Taurine and Sodium periodate)	220nm	242nm	2-10µg/ml	10-50µg/ml	0.62	0.86	2.25	5.11	[7]

2. HIGH PERFORMANCE LIQUID CHROMATOGRAPHY METHOD

Table 3: **Comparative table for Voglibose (VGB) using HPLC**

Mobile Phase (v/v)	Stationary Phase	Linearity (µg/ml)	LOD (µg/ml)	LOQ (µg/ml)	RT	Ref.
Acetonitrile and water (50:50)	C18 (250 x 4.6 mm, 5 µm) column	10-100	2.91	9.7	3.264 min	[8]
0.025M potassium dihydrogen phosphate p^H 2.5: acetonitrile:methanol (40:55:5)	Hibar RT column (250×4.6mm)	100 – 500	30	100	2.6 min	[9]
Acetonitrile: water (20:80 v/*v*)	Agilent TC C18 (250 × 4.6 mm) 5µm column	10-70	0.037	0.114	3.17±0.1 min	[10]
Acetonitrile: water (70:30 v/v)	C18 column (250 mm x 4.6 mm, 5 µm)	10-60	0.054	0.16	3.08 min	[11]

Table 4: Comparative table for Voglibose (VGB) in combination using HPLC

Mobile Phase(v/v)	Stationary Phase	Linearity (µg/ml)		LOD (µg/ml)		LOQ (µg/ml)		RT (min)		Ref.
		VGB	MET	VGB	MET	VGB	MET	VGB	MET	
0.02M KH_2PO_4 : ACN (50:50 v/v)	Hypersil BDS C18 column (250×4.6, 5 µm)	0.3-0.18	50-300	–	–	–	–	0.060 - 3.180	1.947 - 1.960	[12]
ACN : buffer p^H - 6.5 (62:38 v/v)	C18:250X4.6mm, 5µ,amino SS Column	0.30-0.90	500-1500	–	–	–	–	15.02-15.20	4.27 - 4.50	[13]
Buffer: ACN (380:620)	C18:250X4.6mm, 5µ,amino SS Column	0.30-0.90	500-1500	–	–	–	–	15.00-15.20	4.27 - 4.55	[14]
Phosphate Buffer (p^H-6.5) : ACN = 65 : 35	Waters ODS (C18) RP Column, 250 mm x 4.6 mm	10-60	5-40	0.06	0.08	0.18	0.24	–	–	[15]

KH_2PO_4 Buffer, p^H 3.5: Methanol (30:70%v/v)	Hypersil BDS C18 (250mm x 4.6mm, 5µm)	RPG	VGB	RPG	VGB	RPG	VGB	RPG	VGB	[16]
		7.5 - 22.5	4.5 - 13.5	0.541	0.386	1.639	1.171	3.670	5.333	

✓ **solution A** 0.02 M Phosphate buffer adjusted to p^H 2.5 using dilute orthophosphoric acid ✓ **solution B** Diluent: Water: acetonitrile (50:50).	Inertsil ODS 3V (150 × 4.6 mm, i.e. 5 µm) column	MET	VGB	GLI	MET	VGB	GLI	MET	VGB	GLI	MET	VGB	GLI	[17]
		200-600	0.08 - 0.24	0.8-2.4	0.05	0.004	0.002	1.5	0.012	0.006	2.423	8.191	11.708	

0.1% v/v acetonitrile: triethylamine (30:70, v/v)	cosmosil C18 (4.6×250mm, 5µm) with Autochro-3000 software	**MET**	**VGB**	**PIO**	**MET**	**VGB**	**PIO**	**MET**	**VGB**	**PIO**	**MET**	**VGB**	**PIO**	[18]
		200-600	0.08-0.24	30-90	5.45	0.0032	0.93	16.52	0.0097	2.83	2.74	10.10	4.82	
Phosphate buffer (p^H 4.0) and methanol (30:70)	Cosmosil BDS C18 (15 cm × 0.46 cm id, 5µm particle size)	**MGN**	**VGB**		**MGN**	**VGB**		**MGN**	**VGB**		**MGN**		**VGB**	[19]
		25-75	0.5-1.50		2.002	0.053		6.069	0.163		3.580		5.233	
Acetonitrile: Potassium dihydrogen Phosphate buffer (0.01 M, p^H 4), (85:15 v/v)	ODS C18 column (250mm)	**MET**	**GLM**	**VGB**	**MET**	**GLM**	**VGB**	**MET**	**GLM**	**VGB**	**MET**	**GLM**	**VGB**	[20]
		10– 60	2 - 12	1– 6	0.6447	0.0637	0.5854	0.8100	0.1931	0.7176	5.1	3.8	0.8100	

3. HYPHENATION TECHNIQUES

Table 5: Comparative table for Voglibose (VGB) using Hyphenated Techniques

<table>
<tr><th colspan="2">Mobile Phase(v/v)</th><th colspan="2">Stationary Phase</th><th colspan="2">Linearity (µg/ml)</th><th colspan="2">LOD (µg/ml)</th><th colspan="2">LOQ (µg/ml)</th><th colspan="2">RT</th><th>Ref.</th></tr>
<tr><td colspan="2">✓ solution A (1 mL of formic acid in 1000 mL of water) and
✓ solution B (1 mL of formic acid in 1000 mL of methanol)
in the ratio of 50:50</td><td colspan="2">Waters X Terra MS C18, 100 mmx2.1
id, 5 µm column</td><td colspan="2">25.0-1200</td><td colspan="2">1.5</td><td colspan="2">3.0</td><td colspan="2">2 min</td><td>[21]</td></tr>
<tr><td>LC-VD</td><td>LC-MS</td><td>LC-VD</td><td>LC-MS</td><td>LC-VD</td><td>LC-MS</td><td>LC-VD</td><td>LC-MS</td><td>LC-VD</td><td>LC-MS</td><td>LC-VD</td><td>LC-MS</td><td rowspan="2">[22]</td></tr>
<tr><td>Buffer (0.01M mixture of sodium di hydrogen orthophosphate and disodium hydrogen orthophosphate, p^H 6.0) and acetonitrile in 35:65 v/v ratio</td><td>95:5 v/v mixture of 0.01% formic acid and methanol</td><td>Novapak C18 (300×3.9mm , 4µm) column</td><td>Venusil XBPPH (150×4.6 mm, 5µm) column</td><td>20–30</td><td>–</td><td>–</td><td>–</td><td>–</td><td>–</td><td>6.4 min</td><td>–</td></tr>
<tr><td>LC–FD</td><td>LC–MS</td><td>LC–FD</td><td>LC–MS</td><td colspan="2" rowspan="2">50 – 1000</td><td>LC–FD</td><td>LC–MS</td><td>LC–FD</td><td>LC–MS</td><td colspan="2" rowspan="2">4.93 min</td><td rowspan="2">[23]</td></tr>
<tr><td>Acetonitrile and 30mM NaH2PO4 (p^H 6.5) (2:1, v/v)</td><td>10mM aqueous NH_4OAc and acetonitrile (3:7, v/v)</td><td colspan="2">Cosmosil® 5NH2-MS column (150mm×4.6 mm, 5µm)</td><td>9.4</td><td>18</td><td>29</td><td>52</td></tr>
</table>

4. ULTRA PERFORMANCE LIQUID CHROMATOGRAPHY METHOD

Table 6: Comparative table for Voglibose (VGB) in combination using UPLC

Mobile Phase (v/v)	Stationary Phase	Linearity (µg/ml)			LOD (µg/ml)			LOQ (µg/ml)			RT (min)			Ref.
		MET	GLM	VGB	MET	GLM	VGB	MET	GLM	VGB	MET	GLM	VGB	
Buffer (p^H 3.0): Methanol (70:30v/v).	Inertsil ODS (50 x 1.7mm, 3 µm,)	300-700	0.6-1.4	0.12-0.28	2.98	2.95	2.97	9.97	9.97	9.98	0.903	2.619	3.818	[24]

CONCLUSION

UV, HPLC, UPLC, and LC-MS methods have all been reported for estimating Voglibose in bulk and pharmaceutical formulations. As a result of this review, readers will be able to better understand the analytical methodology presented for quantifying Voglibose.

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