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FORMULATION AND IN-VITRO EVALUATION OF VOGLIBOSE DISPERSIBLE TABLETS

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ABSTRACT
The primary objective of this study was to prepare dispersible tablets of Voglibose in two different strengths of 0.2 and 0.3 mg respectively. Voglibose is an oral hypoglycemic drug used effectively in the treatment of type-2 diabetes mellitus. These tablets were prepared by direct compression method using Croscarmellose sodium as a super disintegrant and Orange DC 100 PH was used as a flavouring agent in these tablets. The prepared tablets were evaluated for various physicochemical parameters such as flow properties, hardness, weight variation, thickness, friability, disintegration time, in vitro dissolution studies, assay and uniformity of content. These tablets were also subjected for real time and accelerated stability studies as per ICH guidelines. These tablets were found to be stable even after 6 months of stability study as all the parameters were within limit as per the specifications of Indian Pharmacopoeia.

KEYWORDS: Voglibose, dispersible tablets, direct compression, hypoglycemic, diabetes.

INTRODUCTION
Voglibose is an alpha-glucosidase inhibitor used for lowering post-prandial blood glucose levels in people with type-2 diabetes mellitus. It reduces intestinal absorption of starch, dextrin, and disaccharides by inhibiting the action of α-glucosidase in the intestinal brush border. Inhibition of this enzyme catalyzes the decomposition of disaccharides into monosaccharides and slows the digestion and absorption of carbohydrates. α Glucosidase inhibitors do not stimulate insulin release and therefore do not result in hypoglycemia. Usually, voglibose tablets are orally administered in a single dose of 0.2 mg, 3 times a day, before each meal as it's poorly absorbed. If the effect is not sufficient, the quantity of a single dose may be increased up to 0.3 mg.

In this study, voglibose tablets were formulated in the form of dispersible tablets. Dispersible tablets are uncoated or film-coated tablets that produce a uniform dispersion in water and may contain permitted flavouring and sweetening agents. These tablets generally should be dispersed in water before administration. Dispersible tablets are convenient for the patients who have difficulty in swallowing.

MATERIALS AND METHODS
The following raw materials were used for preparing 0.2 and 0.3 mg strengths of voglibose dispersible tablets and the method used was by direct compression. In the direct compression method of tablet production, dry ingredients are thoroughly mixed and then compressed into tablets. This eliminates the drying steps associated with the wet granulation method. It also reduces the higher costs involved in wet granulation including increased equipment, labor, time, process validation and energy expenditure. As a result, direct compression is both efficient and economical, well suited to the production of high quality tablets, which exhibit hardness, low friability and excellent dissolution rates. As an added benefit, direct compression can improve the physical and chemical stability of tablets as compared to wet granulation.

Table 1: Raw materials, specification, quantity and their uses in tablets

S.No.	Raw Materials	Specification	Quantity (mg/tablet)	Quantity (mg/tablet)	Uses
1.	Voglibose	IP	**0.200**	**0.300**	Active ingredient
2.	Mannitol	IP	60.00	60.00	Diluent & Sweetening agent
3.	Microcrystalline Cellulose PH 102	IP	40.80	40.70	Diluent
4.	Croscarmellose Sodium	USP	5.00	5.00	Disintegrant
5.	Orange DC 100 PH	IH	1.60	1.60	Flavouring agent
6.	Magnesium Stearate	IP	1.20	1.20	Lubricant
7.	Aerosil	IP	1.20	1.20	Glidant
	Total Weight		**110.00**	**110.00**	

Sieving, Mixing & Lubrication: Voglibose was sieved through mesh 100 (#100); mannitol, microcrystalline cellulose PH 102, croscarmellose sodium and orange DC 100 PH were sieved through mesh 40 (#40). Voglibose was first mixed geometrically with mannitol and then with all other excipients manually in a polybag for 5 minutes.

Magnesium Stearate and Aerosil were sieved through mesh 60 (#60) and lubrication was done with the above mixed powder manually in a polybag for 45 seconds. The moisture content of the lubricated powder was observed in Denever digital moisture analyzer at 105°C. The pre-compression parameters of the bulk lubricated powder were performed using Electrolab Tapped Density Tester USP. The pre compression parameters revealed good flow property of powder for both 0.2 and 0.3 mg of voglibose tablets.

Table 2: Pre-compression parameters of bulk lubricated powder

S.No.	Experiment	Result of Voglibose 0.2 mg	Result of Voglibose 0.3 mg
1.	Moisture Content (105^0C)	3.29%	3.36%
2.	Angle of Repose (Ɵ)	$31^0$34’	$31^0$19’
3.	Bulk Density	0.46 g/cc	0.48 g/cc
4.	Tapped Density	0.54 g/cc	0.56 g/cc
5.	Carr’s Index	14.81%	14.29%
6.	Hausner’s Ratio	1.17	1.17

COMPRESSION

After performing the pre-compression parameters the lubricated powder was subjected for punching using Accura 9 station rotary tablet punching machine. The punching tools used were round, biconvex, 6.5 mm plain punch. The machine RPM was 15. The average punch weight of the tablets was 110 mg. The hardness, thickness, weight variation and friability of the punched tablets were maintained in the desired range.

Hardness: Tablets require a certain amount of strength or hardness to withstand mechanical shocks of handling in manufacturing, packing and shipping. The hardness of the tablets was maintained between 60 to 90 Newton. Hardness was measured using digital Campbell Electronics tablet hardness tester.

Thickness: The thickness of tablets should be maintained to overcome packing problems. The thickness of punched tablets was maintained in the range of 3.1 to 3.3 mm with the average thickness of 3.15 mm. Thickness was measured using Dial Vernier Caliper.

Weight Variation: The average percentage weight variation was within ±7.5% i.e. in the pharmacopoeia limit.

Friability: The friability test was performed using Aastha International Tablet Friability Tester. This is important to know the mechanical strength of tablets while handling. The friability of the punched tablets was found to be 0.13% and 0.15% for voglibose 0.2 mg and 0.3 mg tablets respectively.

Disintegration: Disintegration time of the punched tablets was done using Veego Disintegration Test Apparatus. One tablet was placed in each of the 6 tubes of the basket and disintegration was carried out using water maintained at 24° to 26°C. The time taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded. The minimum disintegration time was 20 seconds and the maximum disintegration time was 35 seconds for these tablets. The average disintegration time was 25 seconds.

Uniformity of dispersion: 2 tablets were taken and placed in a beaker containing 100 ml of water with gentle stirring until complete dispersion. A smooth dispersion was obtained for both 0.2 and 0.3 mg tablets of voglibose which passed easily through a sieve screen with a nominal mesh aperture of 710 µm (#22).

Assay: Assay was carried out by liquid chromatography using auto sampler HPLC of Shimadzu as per the method below:
Mobile phase: 0.05M ammonium acetate and Acetonitrile (15:85).
Test solution: 20 tablets were weighed and powdered using mortar and pestle. A quantity of powder was dispersed in the mobile phase with the aid of ultrasound for 60 minutes and diluted with mobile phase to obtain a solution containing 0.004% w/v solution of voglibose.
Standard solution: A 0.004% w/v solution of voglibose RS was prepared using mobile phase.
Column: a diol column 15 cm x 3.0 mm, 5 µm
Flow rate: 1ml per minute
Detector: Refractive Index detector at 50^0
Injection volume: 100 µl

RESULT
For voglibose 0.2 mg tablets the assay value was 0.201 mg (100.50%) and for voglibose 0.3 mg tablets the assay value was found to be 0.299 mg (99.67%).

Uniformity of content: This test was performed for 10 individual tablets employing the same method as described under assay with the following modifications.

Disperse 1 tablet in 4 ml of the mobile phase with the aid of ultrasound for 45 minutes and dilute to volume to obtain a concentration similar to that of the reference solution.

RESULT
96.54 to 102.05% (for voglibose 0.2 mg tablets) and 97.65 to 101.20% (for voglibose 0.3 mg tablets).

In-vitro dissolution: Dissolution was carried out by using water as dissolution medium. A suitable volume of the sample was withdrawn at the end of 15 minutes and filtered. First few ml of the filtrate was discarded and diluted to a suitable volume with water. The absorbance of the resulting solution was measured at the maximum of about 282 nm. The dissolution parameter was maintained as below:
Apparatus: Paddle
Medium: 900 ml of distilled water
Speed: 50 RPM
Temperature: $37^0C \pm 0.5^0C$
Time: 15 minutes
Detection wavelength: 282 nm
Result: Drug release was found to be more than 90% for both the strengths of voglibose tablets.

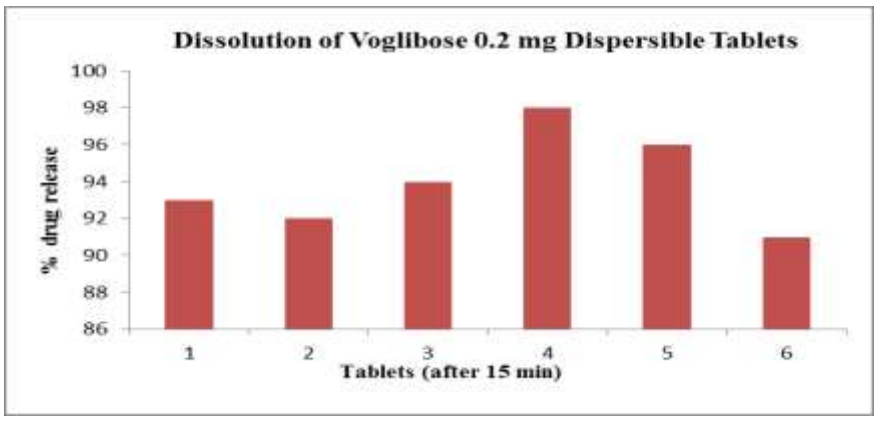

Fig. No. 1 Dissolution of Voglibose 0.2 mg dispersible tablets

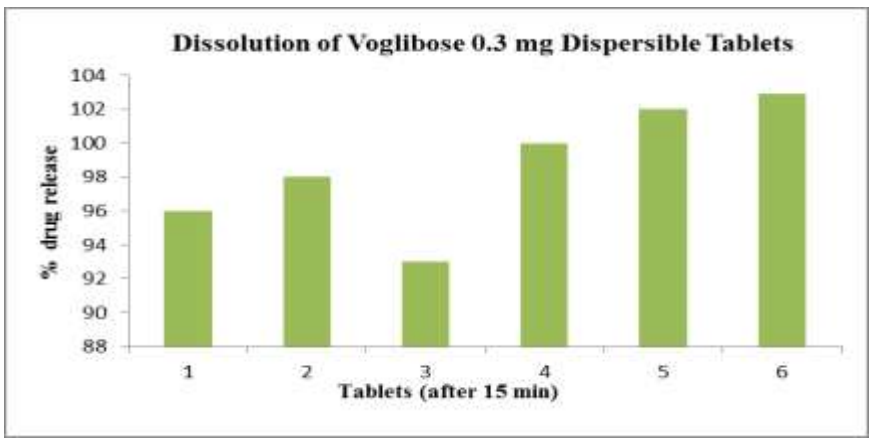

Fig. No. 2 Dissolution of Voglibose 0.3 mg Tablets

Table 3: Summary of Post-compression parameters

S.No.	Test	Result (voglibose 0.2 mg tablets)	Result (voglibose 0.3 mg tablets)
1.	Hardness	60 to 90 Newton	65 to 90 Newton
2.	Thickness	2.6 mm average thickness	2.6 mm average thickness
3.	Weight Variation	Between 105 to 115 mg	Between 106 to 114 mg
4.	Friability	0.13%	0.15%
5.	Disintegration	25 seconds on average	25 seconds on average
6.	Dissolution	91.00 to 98.08%	93.45 to 102.06%
7.	Assay	100.50%	99.67%
8.	Uniformity of Content	96.54 to 102.05%	97.65 to 101.20%

Packing: The primary packing of these tablets was done in Alu-Alu blister. 10 tablets were packed in each Alu-Alu blister.

Stability Studies: After blister packing, these tablets were subjected for real time and accelerated stability studies as per ICH guidelines for 6 months. The real time stability was carried out by storing the tablets at 30°C ± 2°C and 75% ± 5% RH. The accelerated stability was carried out by storing the tablets at 40°C ± 2°C and 75% ± 5% RH.

Table 4: Summary of stability report

Duration (months)	Storage condition	Colour	Average weight (mg)	DT (sec)	Hardness (N)	Assay (%)	Dissolution (%)
1	Acc	White	111.55	20	99 to 116	101.68	86 to 102
3	Real	White	112.00	30	94 to 112	101.50	84 to 105
3	Acc	White	111.70	48	90 to 110	100.08	85 to 101
6	Real	White	111.95	35	98 to 115	101.87	88 to 103
6	Acc	White	110.35	25	89 to 105	100.33	82 to 100

CONCLUSION

Dispersible tablets of voglibose were successfully formulated by employing direct compression method using croscarmellose sodium as a super disintegrant. Pre-compression parameters such as bulk density, tapped density, Carr's Index, Hausner's ratio and angle of repose was done for the bulk lubricated powder and this revealed good flow and compressibility property of the bulk powder. Post-compression parameters such as hardness, thickness, weight variation, friability, disintegration, assay and uniformity of content was performed on punched tablets and all the parameters was found to be within limit as per the limit specified by Indian Pharmacopoeia. Real and accelerated stability study was carried out for a period of 6 months as per ICH guidelines and the formulation was examined for physical appearance, average weight, disintegration time, hardness, assay and dissolution. All the tests showed satisfactory results according to Indian Pharmacopoeia specifications.

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