WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 12, 902-908. Research Article ISSN 2277– 7105

FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLETS OF AN ANTIDIABETIC DRUG

Megha N. Karemore*, R.C. Gulwade, D.R. Mundhada and S. Bhaskaran

Agnihotri College of Pharmacy, Bapuji Wadi, Ramnagar, Wardha 442001, Maharashtra, India.

Article Received on
04 Oct. 2016,

Revised on 24 Oct. 2016,
Accepted on 15 Nov. 2016

DOI:10.20959/wjpr201612-7459

***Corresponding Author**
Megha N. Karemore
Agnihotri College of Pharmacy, Bapuji Wadi, Ramnagar, Wardha 442001, Maharashtra, India.

ABSTRACT

To improve patient compliance, mouth dissolving tablets have emerged as an alternative to conventional dosage form. Voglibose is an alpha glucosidase inhibitor given alone or in combination with sulphonylurea for treatment of type 2 Diabetes to control the post prandial blood glucose levels. During this therapy, it is observed that blood glucose levels are increased. Therefore mouth dissolving tablets of voglibose were prepared to overcome this unusual problem and to make use of the inherent advantages of the novel drug delivery system. Voglibose with sodium starch glycolate, cross carmellose sodium and indione 414 were tableted to obtain mouth dissolving tablets. Voglibose tablets containing 10% indion 414 showed maximum drug release and comparable *in-vitro* release profile as that of marketed formulation. Formulations were subjected to stability studies. Formulations were stable for 4 weeks at 40^0 C with insignificant change in hardness, friability, disintegration time and *in-vitro* drug release pattern.

KEYWORDS: Voglibose, mouth dissolving tablet, sodium starch glycolate, cross carmellose sodium, indion 414.

INTRODUCTION

Oral drug administration has been one of the most convenient and widely accepted routes of delivery for most of the therapeutic agents.[1] However, though popular, this route is not free from limitations of absorption and bioavailability in the lumen of gastrointestinal tract.[3] Various dosage forms like tablets, capsules and liquid preparations have been administered by oral route. But, due to some unsuitable physiological conditions of the gastro-intestinal tract like relatively poor absorption and first pass metabolism by hepatic enzymes, the

administration of some drugs is affected. Also, it limits many drugs to reach into the therapeutic level. Hence, to minimize the problems associated with drug- absorption through gastro-intestinal membrane, researchers have been developing intraoral drug delivery systems that will enhance the therapeutic drug level, avoids first-pass and gut-wall metabolism, increases the bioavailability of active medicament or improve convenience of dosing. Therefore, to cater the needs of such patients, recent advancements in technology have resulted in development of viable dosage alternatives popularly known as mouth dissolving tablets[4] (MDTs). These dosage forms are preferable alternative for oral medication in improving the quality of life and patient acceptability. MDTs are also known as orodispersible tablets, mouth dissolving tablets, rapimelts, melt-in-mouth tablets, fast disintegrating tablets and rapid dissolving tablets.[6] MDTs are the solid unit dosage forms/entities containing medicinal substances which disintegrate or dissolve rapidly in oral cavity usually within a few seconds even without the need of water or chewing. As the tablet disintegrates in mouth, this can enhance the clinical effect of drug through pregastric absorption from the mouth, pharynx and esophagus. In such cases, bioavailability of drug is significantly enhanced by avoiding first pass hepatic metabolism than those observed with conventional tablets. MDTs also combine the advantages of both liquid and conventional tablet formulations allowing the ease of swallowing in the form of liquid.[2,5] The advantages of these dosage forms are continuously and increasingly being identified in both pharmaceutical industries as well as in academia.[7] The objective of present study is to develop the MDT of an antidiabetic drug, Voglibose an alpha glucosidase inhibitor drug and thereby imparting the significance, ideal characteristics and various aspects related to mouth dissolving tablet formulation as a superior dosage form in treatment of diabetes and to improve the patient compliance.

MATERIALS AND METHOD

Voglibose was received as gift sample from Ranbaxy laboratories Ltd. Pharma manufacturing Dewas, M.P. Microcrystalline cellulose (Avicel PH 102) and Sodium starch glycolate received as gift sample from Maple biotech, Pvt Ltd, Pune. Indion 414 received as gift sample from Ion exchange India Ltd. Mumbai. Croscarmellose sodium and Aspartame were received as gift sample from Cipla Ltd. Mumbai. Sodium Periodate and Taurine were procured from Merck chemicals, Mumbai. Magnesium stearate and Talc were purchased from, S.D.fine Chemicals Mumbai. Methanol LR was purchased from S.D. Fine Chemicals Mumbai.

Preparation of MDTs by direct compression method

Mouth dissolving tablets were formulated by employing direct compression method using 8mm biconcave punches. It is the process by which tablets are compressed directly from mixtures of the drug and excipients without preliminary treatment such as granulation. Pure drug voglibose (0.3 mg), super disintegrants in different ratios as mentioned (Table No.1) and excipients were blended using mortar and pestle. The drug and the disintegrants were sieved through mesh # 120 before blending. The granules were evaluated for angle of repose, bulk density and compressibility. The granules were mixed with 1% magnesium stearate as lubricant and 2% aspartame as sweetening agent. Granules were evaluated for precompression parameters like bulk density, angle of repose. The granules were then compressed by using fluidpack rotary tablet machine using 8 mm punch. The hardness was adjusted to 2-4 kg/cm^2. Tablets was evaluated for various parameters like hardness, disintegration time, wetting time and water absorption ratio.

In-vitro dissolution studies

Drug dissolution study was performed on USP type II dissolution apparatus using 100ml phosphate buffer pH 6.8 as dissolution medium. The samples were collected at an interval of 1minutes and absorbance was noted at 282nm.

Drug content determination

The amount of drug equivalent to 3 mg that is 10 tablets were crushed, dissolving the powder mixture in 100 ml of methanol, derivatized by sodium periodate and taurine and suitably diluted with methanol and UV absorbance was measured at 282 nm. Drug concentration was determined from standard graph.

RESULTS AND DISCUSSION

Drug excipient compatibility was studied by FTIR spectroscopy. Results suggest that there was no incompatibility between drug and excipients. Precompression parameters were studied for each formulation. Tablets from each formulation were studied for their physicochemical parameters like hardness, tablet dimensions, weight variations, disintegration time, wetting time and water absorption ratio. Sodium starch glycolate showed least disintegration time at low concentration whereas Croscarmellose sodium and Indion 414 showed least disintegration time at higher concentration. *In-vitro* dissolution studies were carried out on each formulation and compared with the dissolution profile of marketed mouth dissolving tablet of Voglibose (Obligo, Abbott). Formulation V9 containing 10% indion 414

showed excellent results in wetting time, higher water absorption ratio and disintegration time was less than marketed tablet and drug release was identical as that of marketed mouth dissolving tablet Obligo. Hence V9 batch was concluded as an optimized formulation.

Table: 1 Formulation of MDTs

INGREDIENTS	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**
Voglibose	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
CCS %	5	7.5	10	-	-	-	-	-	-
SSG %	-	-	-	5	7.5	10	-	-	-
Indion 414 %	-	-	-	-	-	-	5	7.5	10
Microcrystalline cellulose	30	30	30	30	30	30	30	30	30
Lactose monohydrate	108	105	100	108	105	100	108	105	100
Aspartame	2	2	2	2	2	2	2	2	2
Magnesium stearate	1	1	1	1	1	1	1	1	1
	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7
Total (mg)	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**

Table 2: Evaluation of mouth MDTs

Parameter	V1	V2	V3	V4	V5	V6	V7	V8	V9
Hardness	3.6 ±0.3	3.8 ± 0.3	3.6 ±0.2	3.8 ±0.33	3.4 ±0.23	3.8 ±0.3	3.4 ±0.3	3.8 ±0.2	3.8 ±0.1
Thickness (mm)	2.48 ±0.03	2.40 ±0.01	2.38 ±0.02	2.28 ±0.04	2.36 ±0.02	2.38 ±0.02	2.35 ±0.03	2.48 ±0.02	2.31 ±0.02
Diameter (mm)	8.04 ±0.02	8.08 ±0.02	8.07 ±0.03	8.13 ±0.03	8.10 ±0.01	8.13 ±0.03	8.20 ±0.02	8.20 ±0.02	8.10 ±0.02
Friability %	0.89 ±0.02	0.88 ±0.01	0.81 ±0.03	0.68 ±0.04	0.79 ±0.03	0.85 ±0.03	0.88 ±0.03	0.78 ±0.05	0.54 ±0.02
Weight variation	1.34 ±0.5	3.54 ±0.6	3.65 ±0.3	2.34 ±0.8	2.68 ±0.7	2.96 ±0.4	3.6 ±0.5	3.3 ±0.4	3.2 ±0.6
Disintegration time (sec)	34 ±2	30 ±1	28 ±1	30 ±2	32 ±3	40 ±2	40 ±2	38 ±3	27 ±0.3
Wetting time (sec)	38 ± 2	36 ±2	35 ±1	38 ±1	38 ±2	32 ±1	39 ±1	38 ±1	29 ±1
WAR %	60 ±1.33	70.66 ±0.9	86.66±2.6	57.89±3.3	58 ±3.3	60.18 ±2.3	72 ±0.7	80 ±1.3	88.22 ±2.2
Assay (%)	95.08 ±1.34	105 ±2.32	101 ±2.2	99.16 ±1.5	97.50 ±2.4	103.33 ±1.7	105.83 ±2.6	105.83 ±2.4	102.25±1.8

*n = 3

WAR – Water absorption ratio.

Table 3: *In-vitro* dissolution study

% Cumulative release at Time	V1	V2	V3	V4	V5	V6	V7	V8	V9
1 min	17.53 ± 2.3	19.33 ±3.2	29.33 ±4.1	40 ± 1.3	24 ±3.4	17.33 ±2.7	10.33 ±2.4	25.08 ±4.6	33.66 ±5.1
2 min	53.66 ±1.3	36.33 ±2.3	54 ±3.1	72.33 ±3.5	39.66 ± 2.6	37.68 ±3.3	34.66 ±2.5	61 ±1.6	80 ±4.2
3 min	95.33 ±0.3	86.66 ±0.3	97.25 ±0.3	98 ±0.1	73 ±1.3	86 ±2.3	97.33 ±0.5	96.25 ±0.9	98.38 ±1.1
4 min	98.21 ±0.2	91.66 ±1.2			95 ±2.2	96 ±2.1			
5 min		98.72 ±0.2				97.08 ±1.1			

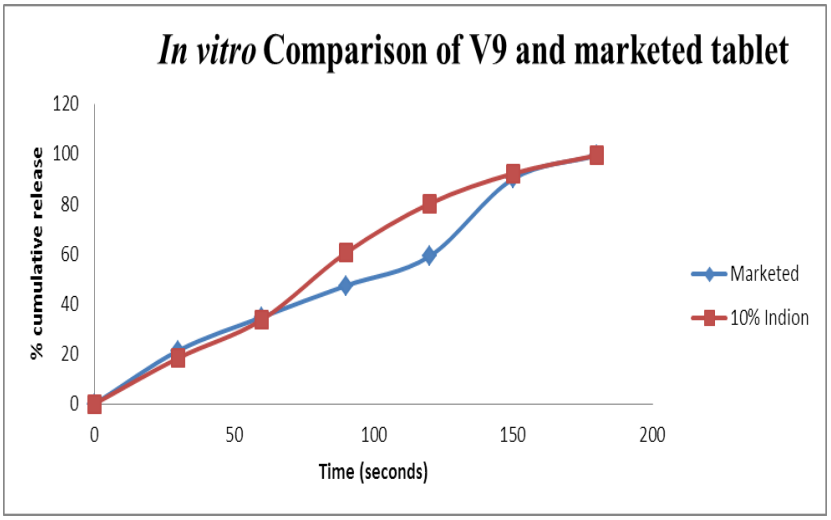

Fig 1: Comparative *In-vitro* release of optimized formulation with marketed tablet

CONCLUSION

Three different superdisintegrants croscarmellose sodium, sodium starch glycolate and Indion 414 were used in formulations. Formulation V9 containing 10% indion 414 has shown the best results for disintegration time of 27 seconds. The disintegration time is less than the marketed mouth dissolving tablet. Water absorption ratio was found to be 88.22% with wetting time of 29 seconds. *In-vitro* dissolution study showed 98.38% of drug release at the end of 3 minutes. The overall results of V9 formulation were excellent. Hence formulation V9 was concluded as an optimized formulation.

ACKNOWLEDGEMENT

This study was carried out at Department of Pharmaceutics, Agnihotri College of Pharmacy, Wardha. The authors are thankful to Ranbaxy laboratories ltd. Dewas, M.P. for providing the gift sample of voglibose and to Shri Shankarprasadji Agnihotri, President of JMSS's, Wardha for providing necessary facilities to carry out this work.

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