An Elsevier Indexed Journal ISSN-2230-7346

Journal of Global Trends in Pharmaceutical Sciences

FORMULATION AND *IN VITRO* CHARACTERISATION OF VILDAGLIPTIN FAST DISINTIGRATING TABLETS

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ARTICLE INFO

Key words:

Vildagliptin,
Croscarmellose Sodium,
Manitol,
Disintegration,
Magnesium Stearate.

ABSTRACT

Vildagliptin, a type-II antidiabetic drug, enhances islet cell insulin secretion via augmented incretin effect. It possesses more affinity for dipeptidyl-peptidase-4 (DPP-4) inhibitor that increases glycaemic control. The usage of vildagliptin results in rapid and complete inhibition of DPP-4 activity. Fast disintegration tablets disperse and dissolve in water within few seconds without leaving any residue and provide the patient the required therapeutic action within few seconds to minutes. In the current study, Vildagliptin disintegration tablets were prepared using direct compression method using three super-disintegrants ie., Croscarmallose sodium, sodium starch glycolate and crosspovidone at different ratios. Disintegration time and dissolution time obtained for the different formulations with different super-disintegrants were compared. Formulated tablets were further evaluated for various parameters like hardness, thickness, wetting time, weight variation and friability. All the parameters were observed within their IP limits. From the results, it was observed that formulations containing sodium starch glycolate disintegrated in a reliable time. Dispersible tablets are particularly formulated for pediatric and geriatric use or for patients who have difficulty in swallowing tablets.

INTRODUCTION

The oral route of drug administration is important method of administering drug for systemic effects. Geriatrics and pediatrics constitute the major part of today's population because of increased lifespan and births. Their impaired swallowing capability makes it a bit difficult for them to receive conventional dosage forms like tablets and capsules. Thus, to overcome this problem, some solid dosage forms were developed that disintegrate or dissolve fast when administered orally without consumption of water. There are different methods for developing fast disintegrating behavior such as molding, lyophilizing and wet compression. As he above said techniques are being time-consuming and require particular machines. In order to overcome all these problems, direct compression technique was adapted for the preparation of fast disintegration tablets as it cheap and convenient way of producing tablets with enough structural integrity. Vildagliptin binds to the catalytic site of DPP-4, elicit long-lasting enzyme inhibition, prevents deprivation of glucagon-like

peptide-1 (GLP-1), and decreases glycaemia in patients among type 2 diabetes mellitus. Superdisintegrants are used to increase the speed of disintegration of tablet. Additional ingredients are used such as coloring agents, flavoring agents and coating agents for the development of tablet. Formulations are designed in small quantities in a laboratory machine called as powder Compaction Simulator machine[3]. Disintegrants or superdisintegrants (e.g. starch or cellulose) are used to uphold wetting and swelling of tablet and it breaks up in gastrointestinal medium; this is necessary for dissolution of API. Main advantage of direct compression is it saves time when compared to another method of compression like wet granulation.

MATERIALS AND METHODS:

Materials:

Vildagliptin(Heterochemicals), Mannitol (LKM International), Crosscarmellose sodium, (Modi Mundi chemicals), Sodium starch glycolate(SSG), Crosspovidone (Hetero chemicals), Megnesium stearate (Yarrow chemicals) and Talc (SD Fine chemicals)

Method of Preparation:

Direct Compression Method

The Vildagliptin dispersible tablets were prepared by using direct compression method with 9mm oval shapes punches and break line on one side of the tablet. The flow chart for direct compression method is given below in following representation.

Procedure:

Ingredients such as Vildagliptin was sifted through 24 mesh, & ingredients such as sodium starch glycolate, crospovidine, Crosscarmellose sodium, mannitol and aspartame, magnesium state, sodium bi carbonate, citric acid,were passed through 60 mesh. The above ingredients were mixed in double cone blender for 25 mins and lubricants were added to the above ingredients. The lubricated blend was compressed by using oval shaped 9.0 punches.

Pre formulation studies:

Vildagliptin standard calibration curve

Serial of dilutions are made from standard solution with distilled water to get concentration from 20 to 100 microgram / ml and the absorbance was measured at 233.0nm.

FTIR studies:

From the figures, it can be seen that, the major functional group peaks observed in spectra of Drug with all polymers remains unchanged as compared with spectra of Vildagliptin**.** From the above IR spectra, it can be observed that there is no interaction between Vildagliptin and Polymers used in formulations.

Bulk density and Tapped density:

The Bulk density of various powder mixed blends prepared with different super disintegrants, was measured by graduated cylinder. The bulk density range 0.401– 0.431 kg/cm^3. The Tapped density of various powder mixed blends prepared with different super disintegrants, was measured by graduated cylinder. The Tapped density was found in the range 0.424 – 0.481 gm/cm^3.

EVALUATION:

Tablets was prepared by direct compression method. The material was free flowing, tablets were obtained of standardized weight due to standardized die fill tablets were obtained in the range with acceptable weight variations as per pharmacopoeia specifications, less than **5%.** Tablets were evaluated by using Vernier calliper. The thickness of tablet was found in the range 5.2 – 6.0 mm. Thickness was obtained due to uniform die fill. Tablets were evaluated by using Pfizer Hardness tester.

Table No 1: Preparation of FDT (F1- F9) by using direct compression method

S.No	Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Vildagliptin	50	50	50	50	50	50	50	50	50
2	PVPK-30	10	10	10	10	10	10	10	10	10
3	Croscarmellose Sodium	10	15	20	-	-	-	-	-	-
4	Cros-povidone	-	-	-	10	15	20	-	-	-
5	Sodiumstarch glycolate							10	15	20
6	Mannitol	127	122	117	127	122	117	127	122	117
7	Magnesium stearate	2	2	2	2	2	2	2	2	2
8	Talc	1	1	1	1	1	1	1	1	1
	TOTAL (mg)	200	200	200	200	200	200	200	200	200

Table no.2 Calibration curve of Vildagliptin

S.No	Concentration (mcg/ml)	Absorbance
1	20	0.114
2	40	0.226
3	60	0.352
4	80	0.470
5	100	0.582

Table no.3 Micromeritic Properties of Granules

S. No	Bulk density (gm/cm^3)*	Tapped density (gm/cm^3)*	Compressibility Index (%)*	Hausner Ratio*	Angle of repose (θ°)*
F1	0.425±0.001	0.464±0.001	8.60±0.001	1.094±0.002	22.33±0.635
F2	0.416±0.006	0.459±0.004	9.36±0.003	1.103±0.001	22.29±1.028
F3	0.425±0.009	0.465±0.002	8.60±0.005	1.094±0.003	24.15±0.350
F4	0.421±0.001	0.459±0.001	8.27±0.007	1.090±0.005	23.48±0.330
F5	0.431±0.004	0.470±0.005	9.57±0.002	1.105±0.002	25.26±0.426
F6	0.425±0.001	0.481±0.002	10.60±0.004	1.118±0.005	22.78±0.203
F7	0.401±0.002	0.462±0.001	9.5±0.002	1.201±0.007	22.48±0.801
F8	0.412±0.006	0.458±0.005	9.06±0.002	1.082±0.002	24.72±0.720
F9	0.419±0.005	0.424±0.004	8.07±0.007	1.063±0.004	21.78±0.210

Table no. 4 Moisture content

Formulation No	Moisture content of the (% w/w)	Formulation No	Moisture content of the (% w/w)
F1	2.1	**F6**	2.7
F2	2.2	**F7**	2.0
F3	1.8	**F8**	1.9
F4	2.2	**F9**	2.4
F5	2.3		

Table no. 5 Assay of Vildagliptin Tablets

Formulation No	Assay of in % w/w
F1	98.3
F2	98.6
F3	99.0
F4	101.7
F5	101.5
F6	102.2
F7	99.03
F8	98.12
F9	100.02

Table no. 6 Stability studies of Vildagliptin tablets.

Parameters	After 15 days	After 30 days	After 45 days
Physical appearance	No change	No change	No change
Weight variation (mg)	200±3.34	200±2.55	200±4.23
Thickness (mm)	5.51±1.87	5.53±2.86	5.54±3.98
Hardness (kg/cm^2)	3.4±0.23	3.3±0.64	3.2±0.99
Friability (%)	0.41±0.05	0.43±0.08	0.43±0.06
Drug content (%/tablet)	100.34±0.34	99.81±0.29	99.01±0.87
Wetting time (sec)	34.19±0.15	39.13±0.45	45.05±0.61
Disintegration time (sec)	58.96±0.41	60.12±0.15	65.51±0.59
Percentage drug release	96.46±0.96	91.36±0.19	85.15±0.15

Graph 1:Standard graph of Vildagliptin

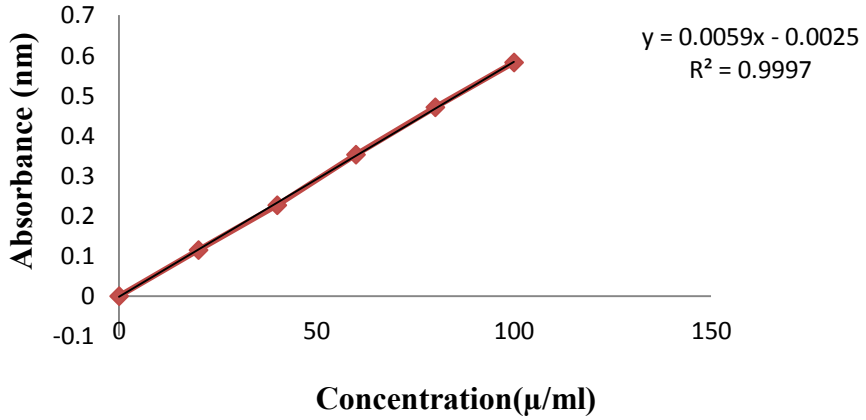

Fig no.1 Standard graph of Vildagliptin

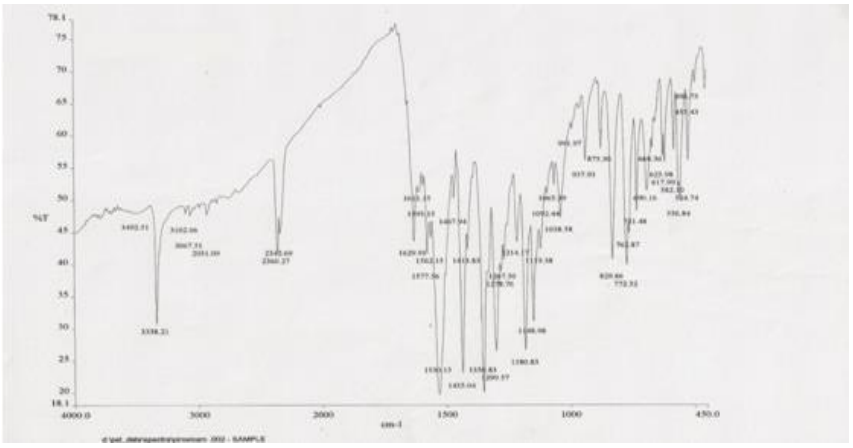

Fig no.2 infra red spectrum of pure vildagliptin

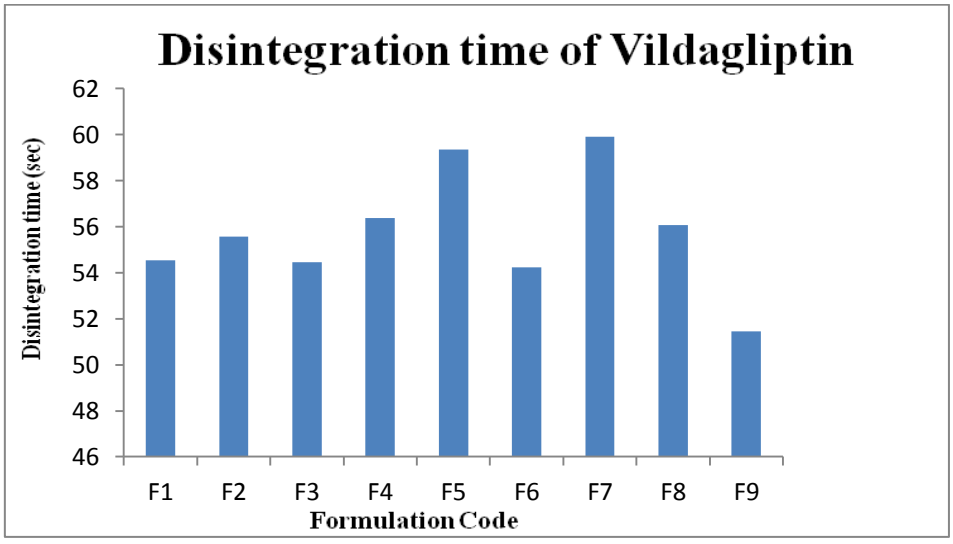

Fig no. 3 Disintegration time of Vildagliptin

Wetting Time of Vildagliptin

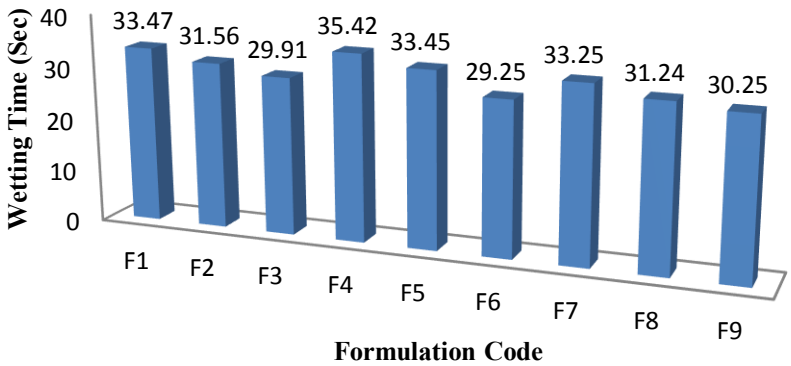

Fig no.4 Wetting Time of Vildagliptin

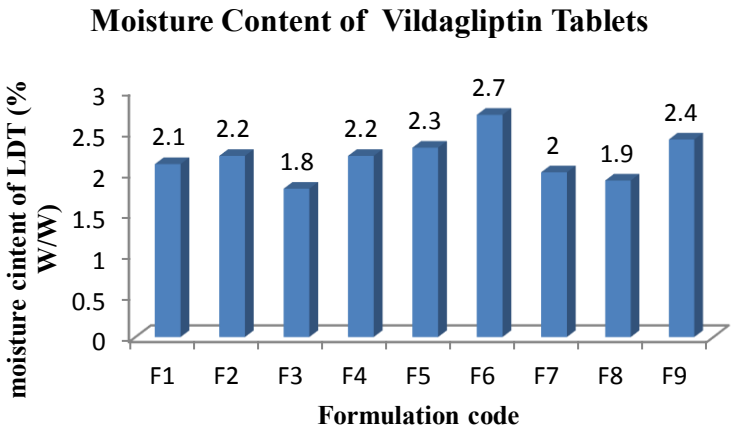

Fig no. 5 Moisture content of Vildagliptin Tablets

Hardness of the tablets was found in the range 3.36 – 3.71 Kg/cm^2**.** Uniform hardness was obtained due to equal compression force. Tablets were evaluated by using Roche Friabilator. Friability of tablets was observed in the range 0.291 - 0.530. Tablets were evaluated for disintegration time in the IP disintegration apparatus. The disintegration time was found in the range 51 – 59 sec. The tablets are evaluated for the uniform dispersion in which all the tablets were dispersed in few seconds in purified water and the formulations were under the IP limits.

Moisture content:

The result of the moisture content of the prepared FDT was done as per the procedure and presented in the table

Assay of Vildagliptin:

The assay of Vildagliptin were done as per procedure and presented in the table. Tablets were evaluated by using assay method. The drug was obtained in acceptable limit. The drug content was found in the range 98.3 – 102.2%.

According to ICH guidelines, 45 days stability study at 4^{0}C ±2^{0}C, 27^{0}C ±2^{0}C and 45^{0}C ±2^{0}C for 45 days at RH 75±5% of optimized formulation (F9) was carried out. It shows significant change over time for parameters like appearance, drug content, dissolution and assay etc., No major difference in drug content between initial and formulations stored at 4^{0}C ±2^{0}C, 27^{0}C ±2^{0}C and 45^{0}C ±2^{0}C for 45 days at RH 75±5% for 45 days.

CONCLUSION:

The present study is an attempt to select best combination of diluents and disintegrants to formulate dispersible tablet of Vildagliptin which disintegrates within few minutes thereby reducing the time and onset of action. Mannitol is selected as diluents, Sodium starch glycolate, Crosspovidone, croscarmellose sodium were selected as super disintegrants , in different concentrations. Aspartame as a sweetening agent, Magnesium stearate as a Lubricant and glidant. From the data obtained, it is observed from the formulation containing Citric acid - 40mg, sodium bi carbonate - 20mg. Formulation F9 shows Disintegration time in 51 seconds and the Percentage drug release is 99.18 % at the end of 10 min which satisfied all the tablet evaluation parameters for dispersible tablet. So for the satisfactory parameters F9 batch is selected as optimized batch.

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