FORMULATION AND EVALUATION OF SUSTAINED RELEASE MATRIX TABLET OF VILDAGLIPTIN FOR THE TREATMENT OF TYPE-2 DIABETES

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Abstract

It was determined that Vildagliptin's sustained release matrix tablets, which use pectin as a release retardant, were effectively designed in order to maintain the drug's release rate. To create Vildagliptin sustained Release pills, the current work centered on "Formulation and Assessment of Vildagliptin Sustained Release Tablets for the treatment of Type-2 Diabetes" was done. There are different types of method we have used to formulate the tablet, including direct compression, Dry Granulation, and Wet Granulation. After the completion of granulation, we have study of Granules Evaluation Test such as loss on drying, fine ratio study, Bulk density, Tapped density, Compressibility Index, and H The physical appearance, shape, size, weight variation, thickness, hardness, dissolution duration, friability, and in-vitro dissolution test were all performed during the compression process. Also, a study of the drug release was conducted. After performing a dissolution study, the percentage of drug release was calculated. Based on evaluation data, Formulation-dissolution F5's profile was optimized. Much of the formulations that were produced were modeled around Higuchi-Peppas' medication release for dissolving. F5 tablet formulation optimization was done after zero order kinetic drug release. Once the developed tablet underwent a three-month stability test in a stability chamber, the results were found to be stable. In this study, it was discovered that pectin significantly influenced the amount of medication Vildagliptin sustained Release tablets released from the matrix system for the treatment of Type-2 Diabetes. As a result, it may be said that the formulation's performance is robust, meaning that it is less likely to be impacted by the many circumstances examined.

Keywords- Vildagliptin, sustained release, matrix tablets, Type-2 Diabetes, Bulk density, Compressibility Index, Higuchi-Peppas etc.

1. INTRODUCTION

The oral route is the most typical way to provide tablets, capsules, and liquid medications to the gastrointestinal tract (GI tract). It may be used to treat and prevent local gastrointestinal disorders as well as deliver systemic and non-systemic medications. Is the most popular choice among patients of all ages since it offers several benefits, including the ability to self-administer and non-invasiveness of the route? It is also possible to build Formulations that are tuned to improve medication delivery to certain parts of the upper or lower GI tract. The mouth, throat, esophagus, stomach, and the first segment of the small intestine (duodenum) make up the majority of the gastrointestinal tract's top portion, while the large intestine and the remaining segments of the small intestine (jejunum and ileum) make up the segment's bottom segment (cecum, colon, and rectum). While tablets typically have a slower rate of absorption after oral administration of drugs, this is not desirable for patients in an emergency. The oral route of drug administration is one of the most widely used methods for getting drugs into the human body system and producing well-tolerated therapeutic results.

Advantages:

- Simple & Convenient to use.
- Drug Readily available by Prescription

Disadvantages:

- Observed the Patient Noncompliance.
- Dosages are sometime largely empirical

Sustained Release Drug Delivery System

Prolonged release dosage forms are fashioned to get produce a chronic therapeutic consequence inside continuing receiving released of medicament over a protracted period amount of time following administration. Most concentrate of manufacturing sustained unharnessed dosage form was designed to modification & increases the medication showing by expand the time of drug action, reducing.

Drug Choice for Sustained SRDDS

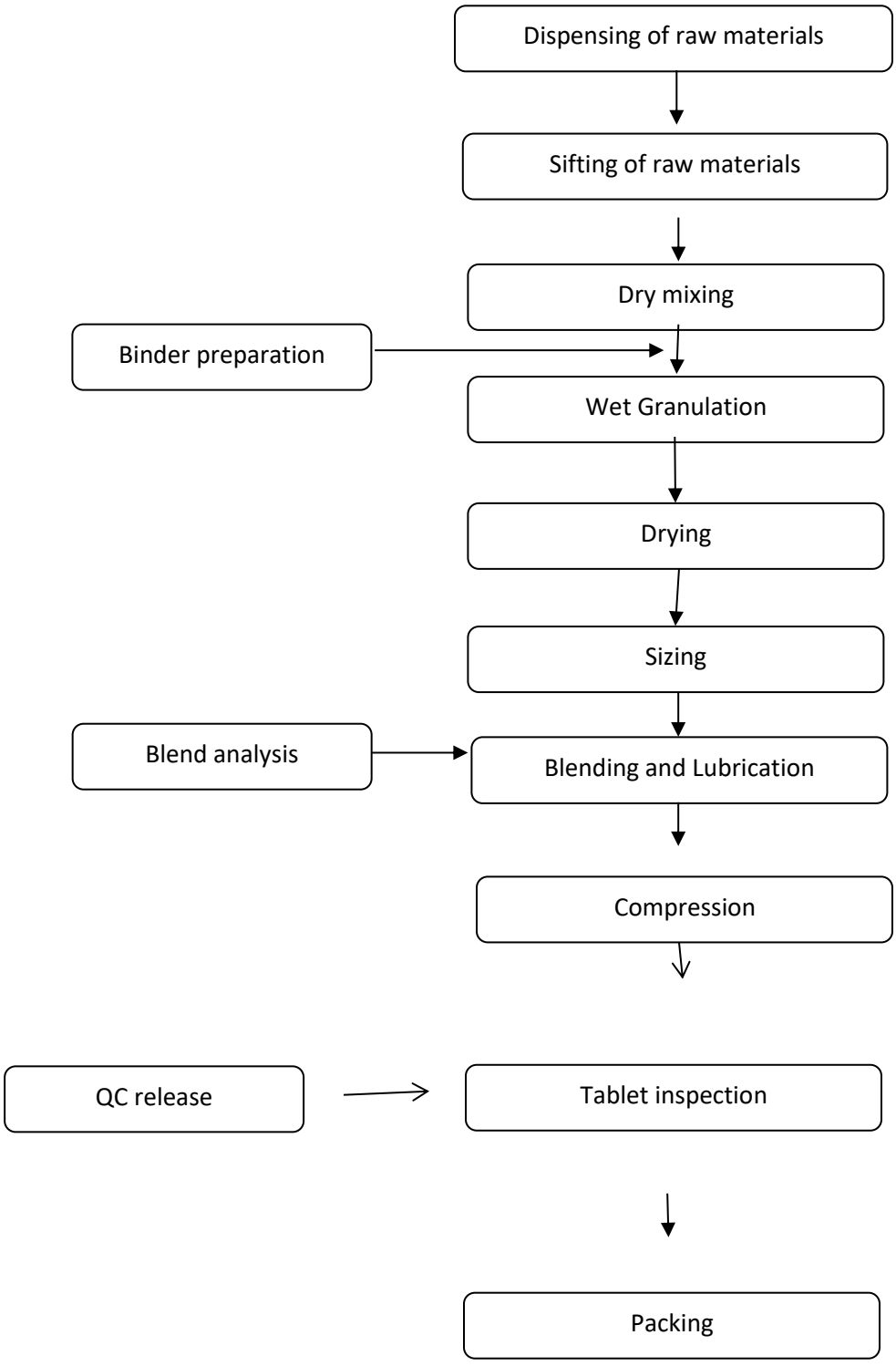
Physiochemical, pharmacokinetic, and pharmacodynamic characteristics of the moiety, anatomical, physio mechanical characteristics of the digestive tract, and physio mechanical characteristics of the drug delivery mode of the dosage form to be designed are some of the basic fundamental knowledge that is required for the scientific development of oral DDS. A unit of physicochemical and pharmacokinetic criteria to the development of a medication in the form of a sustained-release dosage form that affordably incorporates knowledge about the process of a moiety's absorption via the digestive system

2. MATERIAL AND METHOD

Material– The drug Vildagliptin from pulse pharmaceutical Roorkee, Haridwar uk. Microcrystalline cellulose from pulse pharmaceutical Roorkee, Haridwar uk, Pectin from Central drug house (CDH)

Pvt. Ltd, New Delhi, India, Hydroxy propyl methylcellulose from Central drug house (CDH) Pvt. Ltd, New Delhi, India, Magnesium stearate from Central drug house (CDH) Pvt. Ltd, New Delhi, India.

Method-



Vildagliptin 50 mg tablets were created using a variety of granulation techniques, each of which is appropriate for using various types of excipients, including pectin HPMC, with concentrations that may range from 25, 50, 75, 100, or 150 mg depending on the situation. may use varying ratios to optimize various formulations utilizing various synthetic or natural polymers. Take the API and excipients and weigh them using a calibrated balance according to the appropriate requirements for the amount of medicine and polymer. Before dispensing the material, cross-checked the vendor's COA and other specifications. Separated each material & polymer first, then passed each through the specified sieve while holding the binder solution until none of the other materials passed through the sieve save for the lubricant. Take and maintain all materials outside of RMG. Start the chopper for dry mixing for 10 minutes, and then add the binder slowly using a spray gun; this should take 15 to 20 minutes. Start the chopper for 2 minutes, and then turn on the impeller at high speed until the necessary ampacity is not reached. Release the granules from the RMG unit. Milling must be done to get the correct granule size before transferring the granules into the dry FBD. The resulting granules were dried for 20 minutes at 450°C. Check the LOD of the granules after that; if it is within the limit, sieve 20 was used to pass the granules. Granules that are too big are crushed with. 50 mm milling screen in multi mill, then HPMC via sieve, followed by dry mixing of magnesium stearate for 10 minutes, lubricating component, and running blender for 2 minutes, adding to the granules. Next, put the granules in a container with two polybags. If every granule parameter is accurate, move it to the compression area. then compress the double-rotary tableting machine with nine stations. Release the granules from the RMG unit. Milling must be done to get the correct granule size before transferring the granules into the dry FBD. The resulting granules were dried for 20 minutes at 450°C. Check the LOD of the granules after that; if it is within the limit, sieve 20 was used to pass the granules. Using a multi-mill and a.50 mm milling screen, oversized granules are crushed before being passed through a sieve, HPMC, magnesium stearate, and lubricating component before being blended for two minutes and added to the granules. Next, put the granules in a container with two polybags. If every granule parameter is accurate, move it to the compression area. Then compress the double-rotary tableting machine with nine stations.

Drug Polymer Ratio

Drug and polymer with different ratio

Formulation Code	Drug	Pectin	HPMC
F 1	50	50	--
F 2	50	100	--
F 3	50	150	--
F 4	50	25	25
F 5	50	50	50

+ All of the formulation has, MCC,
1% w/w magnesium stearate *wet granulation

Formulation Series:

Formulation Series of Vildagliptin Sustained Release Matrix Tablets

Formulation Code	Drug	Pectin	HPMC	MCC	Mg Stearate	Total
F1	**50**	**100**	**-**	**97.5**	**2.5**	**250**
F2	**50**	**50**	**-**	**147.5**	**2.5**	**250**
F3	**50**	**150**	**-**	**47.5**	**2.5**	**250**
F4	**50**	**50**	**50**	**97.5**	**2.5**	**250**
F5	**50**	**25**	**25**	**147.5**	**2.5**	**250**

3. RESULT

1. Physical appearance-

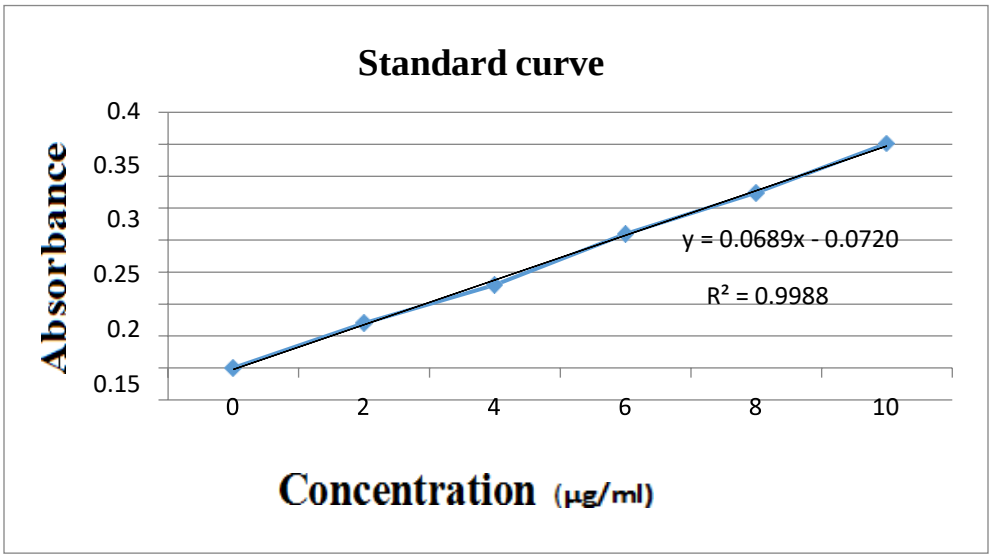
Tablet compressed are white of white round flat faced, beveled edge uncoated tablets plain on both side.

2. UV Spectrophotometric Method for Vildagliptin

Preparation of calibration Curve in 0.1N hydrochloric acid

Calibration Curve data of Vildagliptin in 0.1N HCL

Conc. (µm/ml)	Abs.
2	0.012
4	0.18
6	0.20
8	0.282
10	0.324



Vildagliptin in 0.1N HCl

3. Micrometry Study

Micrometrics properties like tapped density, bulk density, Carr's index etc of whole formulation of sustained release matrix tablet (SRMT) of Vildagliptin were performed &found the relevant data, shown in below table

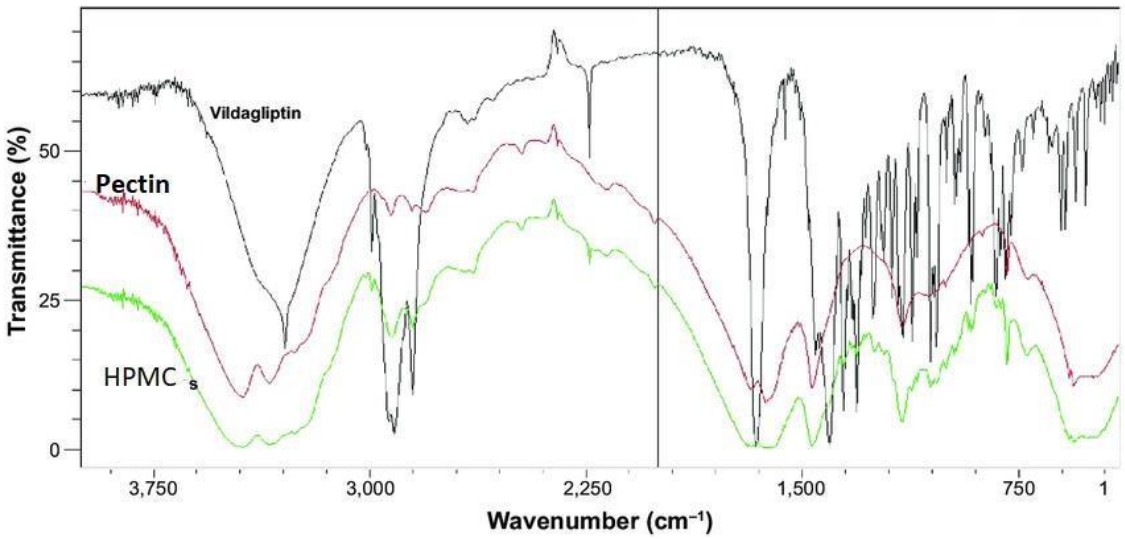
Micrometrics Properties of Sustained Release Matrix Tablet of Vildagliptin

Formulation code (F)	Angle of repose(Ɵ)	Bulk density (gm / cm3)	Tapped density (gm/ cm3)	Carr' index
F1	27.13±0.12	0.42±0.05	0.54± 0.03	1.22± 0.04
F2	29.89±0.13	0.41±0.04	0.48±0.02	1.14±0.05
F3	25.59±0.08	0.43±0.06	0.52±0.05	1.21±0.04
F4	25.45±0.5	0.46±0.08	0.56±0.07	1.23±0.05
F5	30.50±0.03	0.39±0.04	0.46±0.02	1.18±0.05

Mean ± SD (n=3)

4. FTIR

FTIR Spectrum of Drug+ Pectin and HPMC



FTIR Spectrum Analysis

S. No	Frequency, cm ⁻1	Bond	Functional group	Pure drug (Vildagliptin)	Drug+Pectin+HPMC
1	3300-3500	=CH-Stretch	Alcohol	3356.6	3423.4
2	1680-1620	C=O	Alkenyl	1639.53	1637.4
3	920-675	C-H	Aromatics	917.5	946.44

4. EVALUATION PARAMETER

Following compression, physical examinations of the Vildagliptin tablet's (hardness test, weight variation, friability thickness, and drug content) results revealed the pertinent information displayed in the table below.

Various evaluation parameters

Formulation Code (F)	Hardness (NMT 6.0 kg/cm2)	Thicknes(3.20 ± 0.20 mm)	Friability (NMT 1.0%w/w)	Drug uniformity (NLT 80%)	Weight variation (250 ±3 %mg)
F1	6.5	3.20	0.15	99.6	249.2
F2	7.5	3.18	0.12	99.0	252.6
F3	6.9	3.14	0.13	99.0	250.9
F4	6.0	3.12	0.18	99.2	253.6
F5	7.4	3.10	0.15	99.3	247.1

Dissolution Study:

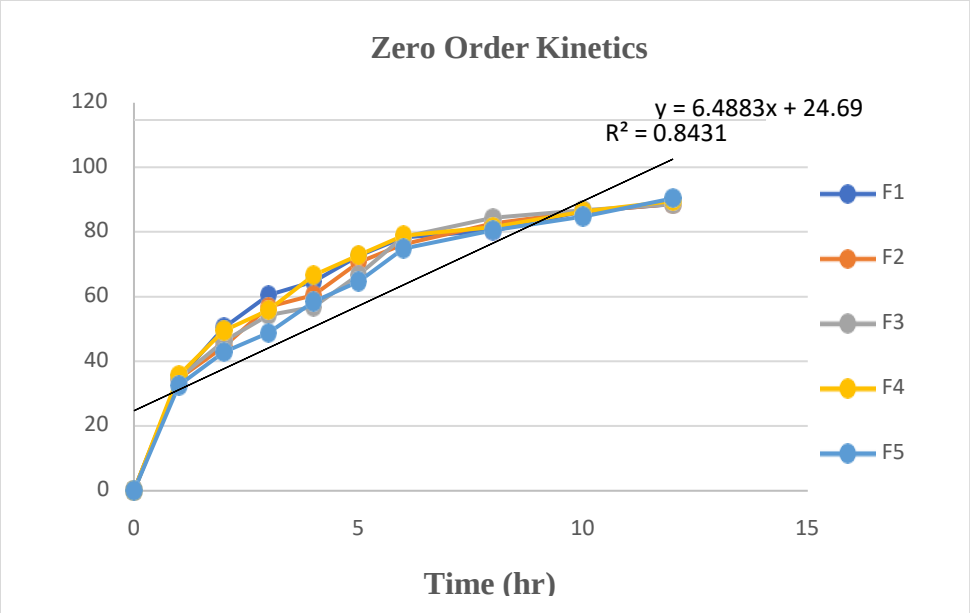
Vildagliptin tablet % drug release testing was done in vitro with various polymer concentrations at various time intervals (between 1 and 12 hours), and the results are shown below.

% Drug Release in 12hrs at 0.1N-HCL Dissolution Medium

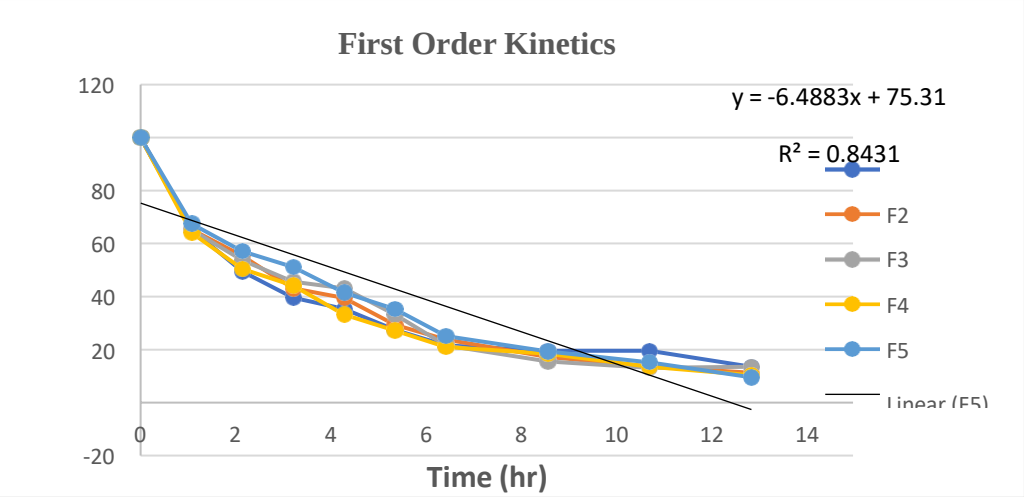
Time	F1	F2	F3	F4	F5
0	0	0	0	0	0
1	34.6±0.10	34.6±0.09	34.8±0.10	35.8±0.16	32.5±0.04
2	50.4±0.11	44.6±0.08	46.2±0.12	49.5±0.14	42.8±0.06
3	60.4±0.15	56.8±0.15	54.3±0.10	55.8±0.12	48.8±0.24
4	64.6±0.14	60.5±0.16	56.9±0.14	66.7±0.14	58.4±0.16
5	72.6±0.12	70.6±0.12	66.8±0.12	72.8±0.08	64.7±0.06
6	78.3±0.17	76.2±0.18	78.4±0.10	78.9±0.14	74.8±0.13
8	80.4±0.8	82.7±0.18	84.4±0.11	81.5±0.08	80.6±0.14
10	86.4±0.4	86.3±0.4	86.8±0.12	86.4±0.07	84.8±0.08
12	88.6±0.4	88.7±0.9	86.4±0.5	89.6±0.8	90.4±0.16

Kinetic Parameters of Optimized Formulation

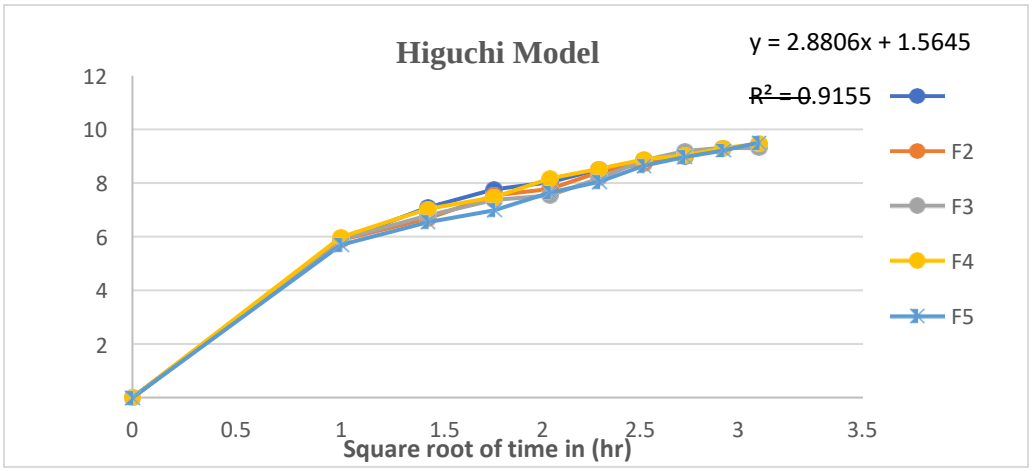
Formulation	0-Order	1st-Order	Higuchi Model	Peppas Model
	R^2	R^2	R^2	R^2
1	0.743	0.7057	0.8718	0.4919
2	0.7905	0.7905	0.878	0.691
3	08034	0.7899	0.8928	0.7447
4	0.757	0.757	0.878	0.785
5	0.8431	0.8431	0.9155	0.5242



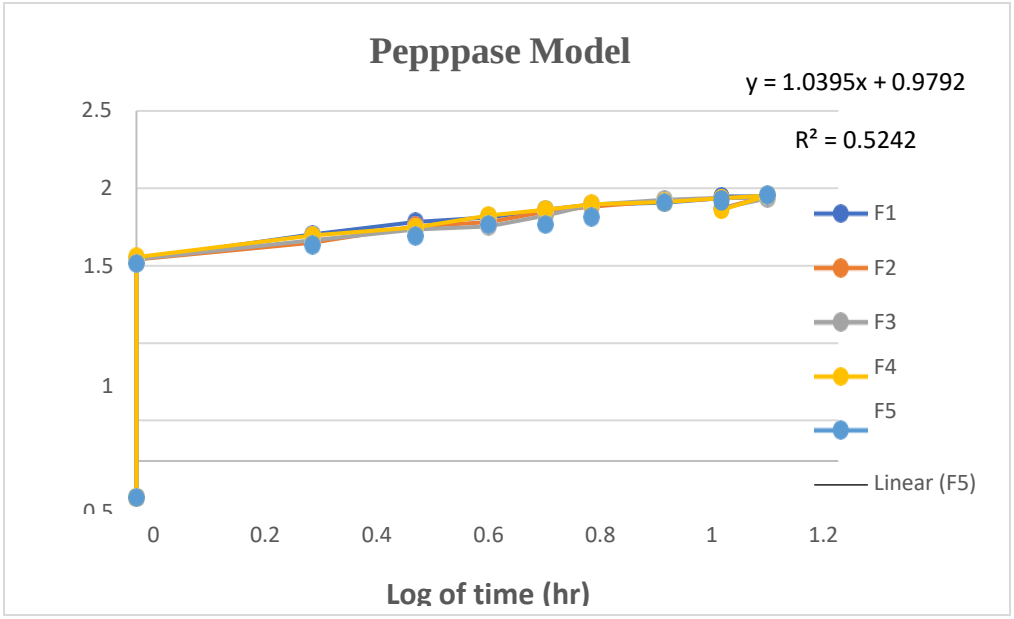
Zero order release kinetic



First order release kinetics



Higuchi model



Peppas Model

Stability Study

Stability Study of best Formulation F5

S. no	Parameter	Initial	1st month	2nd month	3rd month
1	Appearance	White	No change	No change	No change
3	Drug content	99.3	99.3	99.2	99
4	Hardness	6.5	7.5	6.4	6.2
5	Friability	0.20	0.18	0.13	0.14

5. SUMMARY

The creation and assessment of a sustained release Vildagliptin matrix tablet for the treatment of Type-2 Diabetes were the major goals of this effort. Many investigations, including kinetics, stability, and pre-formulation experiments, were carried out with the use of the wet granulation technique. Understanding which polymer would provide the tablets a better matrix shape and aid in prolonged release of the tablets is helpful. The formulation was created utilizing several medication dosages, including pectin (100, 50, 150, 25, and 75), HPMC (50, 25, and 75), for use in future research. To determine angle of repose, bulk density, tapped density, and Carr's index, Vildagliptin tablets go through a preformulation research with several formulations (F1-F5). It displays the pertinent information (F1-F5), including the Angle of repose (25.45-0.06-30.50-0.02), Bulk and Tapped Densities (0.39-0.06 and 0.46-0.09), and Carr's Index (1.14-0.05 and 1.23-0.04).

The most crucial component of the plan is characterization and assessment, which aids in understanding the physical characteristics of the tablet, including its hardness test, friability, weight fluctuation, and thickness. The based information for several formulations (F1-F5), include hardness (4.00.05-4.70.03), thickness (3.820.02-4.200.14), friability (0.260.03-0.330.03), and weight variation (2473.6-2524.1.

Vildagliptin tablet in vitro drug release investigation was carried out with various polymers concentrations (Pectin -100, 50mg 50, 50mg 150, 50mg 25, 50mg 75, 50mg HPMC 50, 50mg 25, 50mg 75, and 50mg) at various times (1to12 hrs). Tablets released a variable proportion of the medicine at each interval; however, after 12 hours, the formulation (F5), which included 75 mg of pectin and 75 mg of HPMC, demonstrated a better sustained release of the drug (90.40.16). It was important to determine the kinetic property in order to determine the composition of the tablet. Data on (F5in)'s vitro drug release were fitted into multiple kinetics models.

6. CONCLUSION

It was determined that Vildagliptin's sustained release matrix tablets, which use pectin as a release retardant, were effectively designed in order to maintain the drug's release rate. To create Vildagliptin sustained Release pills, the current study, "Formulation and Assessment of Vildagliptin Sustained Release Tablets for the Treatment of Type-2 Diabetic," was conducted. Several aspects that may have an impact on the sustained release's performance were examined during this part of the inquiry. A technique for wet granulation was developed. Before being punched into tablets, granules were

subjected to tests for bulk density, tapped density, compressibility index, and Hausner ratio. Tablets had their weight fluctuation, thickness, and friability assessed. An in-vitro dissolving test was also conducted, and the percentage of drug release was examined. Drug release percentages were estimated after dissolution experiments were conducted. Based on assessment data, Formulation-dissolution F5's profile was optimized. All of the generated formulations complied with Higuchi-drug Peppa's release in the dissolution modeling. Drug release in the improved formulation-F5 was zero-ordered. The created formulation passed a three-month stability test with flying colors. In this study, it was discovered that pectin significantly influenced how Vildagliptin sustained Release tablets, used to treat Type-2 Diabetes, and were released from the matrix system. In light of this, it may be said that the formulation is sound since its performance is less likely to be impacted by the many elements examined.

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