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FORMULATION AND EVALUATION OF GASTRO RETENTIVE DRUG DELIVERY SYSTEM OF SITAGLIPTIN

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ABSTRACT

This study aimed to develop a novel gastro-retentive drug delivery system in the form of floating tablets containing the antidiabetic medication sitagliptin. Sitagliptin acts by inhibiting the enzyme dipeptidyl peptidase-4 (DPP-4), which helps break down hormones released by the gut in response to food intake, including glucagon-like peptide-1 (GLP-1).The tablets contains Pectin and HPMC K as binders, with lactose monohydrate serving as a diluent. The effervescent agent, utilizing Citric acid as a gas-generating agent, was the basis for causing the tablet to float. Magnesium stearate and talc are used in this tablet to increase the flow properties of the powder thus it helps in punching of the tablet. The direct compression method facilitated the production of six distinct formulations. Evaluation of these formulations focused on pre compression studies and post compression studies of the tablet. Consistency was observed across all formulations, indicated by minimal weight variation and good in vitro dissolution profiles. Among these formulations, M5 distinguished itself as the most promising. It was composed of 3mg Pectin and 7mg HPMC K, achieving an extended floating duration of 12 hours coupled with an efficient drug release profile over 8 hours. This formulation's performance suggests its potential as an effective gastro retentive delivery system for Sitagliptin, offering a controlled release that could enhance patient compliance and therapeutic efficacy.

Keywords: Floating tablets, Pectin, HPMC K, Citric acid, Sitagliptin, Floating lag time.

INTRODUCTION

The goal of gastroretentive drug delivery tablets is to maximize drug absorption and bioavailability by extending the medication's residence time in the stomach. They accomplish this by attaching themselves to the stomach mucosa, swelling, or creating a buoyant layer, which delays their premature passage into the intestines[1]. Retardant tablets have benefits including lower dosage frequency and better patient compliance since they sustain therapeutic medication levels for longer[2]. Floating Drug Delivery devices are the most innovative devices. Pharmaceutical formulations known as floating effervescent tablets are made to release gases when they exposed to gastric fluids, which causes the fluids to

float on the stomach's surface. Typically, the effervescent ingredients in these pills are sodium bicarbonate and citric acid, which react with stomach acid to form carbon dioxide gas. Tablets float because of the buoyancy these bubbles create.[3] Because of their extended release qualities and simplicity of administration, floating effervescent tablets provide increased bioavailability, decreased dosage frequency, and greater patient compliance[4].

When a person has diabetes mellitus, their glucose levels are raised due to lacking insulin production by the body or improper insulin uptake by body cells. Insulin therapy or medication were utilized to treat diabetes. Under this, type II diabetes mellitus was most common and anti-diabetic medications were the only ones prescribed[5].

The dipeptidyl peptidase-4 (DPP-4) enzyme is inhibited by the medication. Hormones generated by the gut in reaction to food consumption, such as glucagon-like peptide-1 (GLP-1), are broken down with the help of DPP-4. By increasing insulin production and blocking glucagon release, GLP-1 lowers blood glucose levels and aids in blood sugar regulation. Sitagliptin increases the amount of GLP-1 and other incretins in the bloodstream by prolonging their duration of action.

This causes responses to secrete more insulin. Sitagliptin works by blocking the activity of dipeptidyl peptidase-4 (DPP-4). DPP-4 aids in the breakdown of hormones produced by the stomach in response to food consumption, such as glucagon-like peptide-1 (GLP-1). GLP-1 helps to regulate blood sugar by lowering blood glucose levels and promoting the synthesis of insulin while inhibiting the release of glucagon. Sitagliptin prolongs the duration of action of other incretins, such as GLP-1, hence increasing their quantity in the bloodstream. As a result, when blood glucose levels rise, less glucagon is released and more insulin is secreted, which improves glucose management [6, 7].

Materials and Methods

Materials

Sitagliptin was used as active ingredient. Binders like Pectin, HPMC K, floating agent Citric acid, diluent lactose monohydrate, magnesium stearate and talc are used to increase flow properties were used at laboratory grade reagents**.**

Methodology

Preparation of calibration curve for Sitagliptin in 0.1N HCL:

Prepare 0, 2.5, 5, 7.5, 10, 12.5 ,15 µg/mL concentrations of Sitagliptin solution in 0.1N HCL and note absorbance against blank at 266 nm using UV absorption spectrophotometer.

Drug and Excipients compatibility studies using FTIR:

In this FTIR the drug functional groups were identified and Compatibility was observed of these excipients with Sitagliptin[8]

Pre-formulation studies:

Pre formulation studies include drug and flow properties of formulation blends before punching. Flow properties like Bulk density, tapped density, angle of repose, Compressibility index and Hausner's ratio were studied.

Table 1. FORMULATION TABLE FOR SITAGLIPTIN EFFERVESCENT TABLETS

INGREDIENTS:	M1	M2	M3	M4	M5	M6
SITAGLIPTIN (mg)	100	100	100	100	100	100
PECTIN (mg)	7	6	5	4	3	2
HPMC K (mg)	3	4	5	6	7	8
CITRIC ACID (mg)	18	18	18	18	18	18
LACTOSE MONOHYDRATE (mg)	62	62	62	62	62	62
Mg STEARATE (mg)	6	6	6	6	6	6
TALC (mg)	4	4	4	4	4	4
Total Weight (mg)	200	200	200	200	200	200

Fourier Transforms Infrared Spectroscopic Studies (FTIR)

Using an FTIR spectrophotometer and KBr pellets, FTIR spectra for the drug and the excipients will be acquired in order to investigate the interaction and compatibility between excipients and medications. Utilizing the spectrometer, 4000-400 cm-1. Before the KBr is utilized in the KBr press to press pellets for the FTIR research, it will be kept in a hot-air oven for two hours to reduce moisture content. The previously described dried KBr will next be used to prepare the drug pellets and selected formulation excipients. The results of the infrared tests for the medication and powder mixture must to be recorded. [11].

Post compression parameters:

Prepared tablet formulations were studied for Thickness, Hardness, Friability, weight variation, swelling index, Buoyancy studies and In-vitro drug release studies.[12-15]

Results

The physicochemical properties and micromeritics properties of the formulation were performed as per the procedure.

Table.2. Standard calibration curve of Sitagliptin 0.1 N HCl

Concentration	Absorbance
0	0
2.5	0.046
5	0.088
7.5	0.124
10	0.161
12.5	0.203
15	0.246

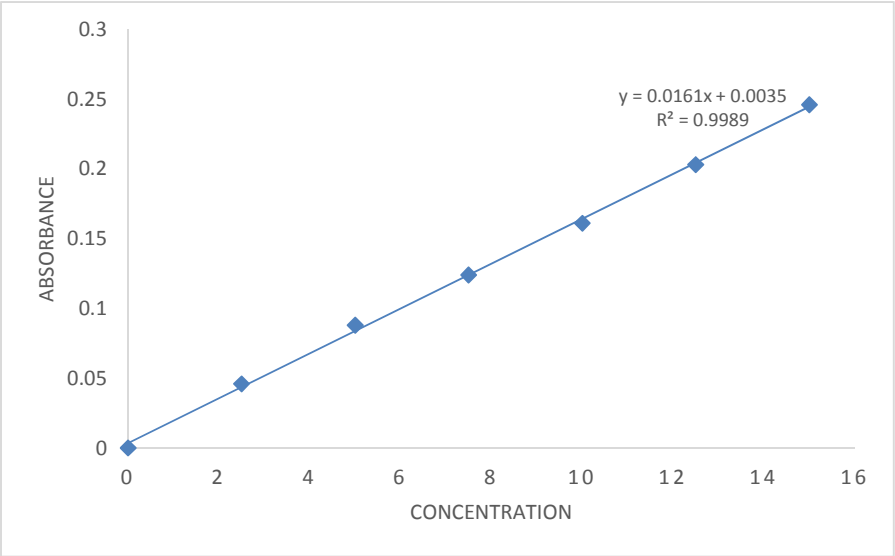

Figure.1. Standard calibration curve of Sitagliptin in 0.1 N HCl Solution

FTIR Spectroscopy Study

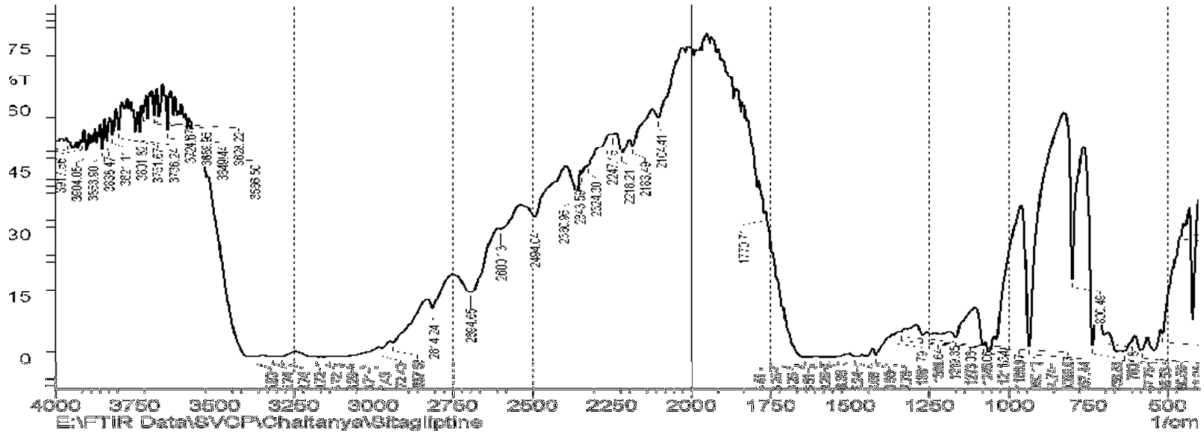

Fig .2: FTIR spectra of pure drug Sitagliptin

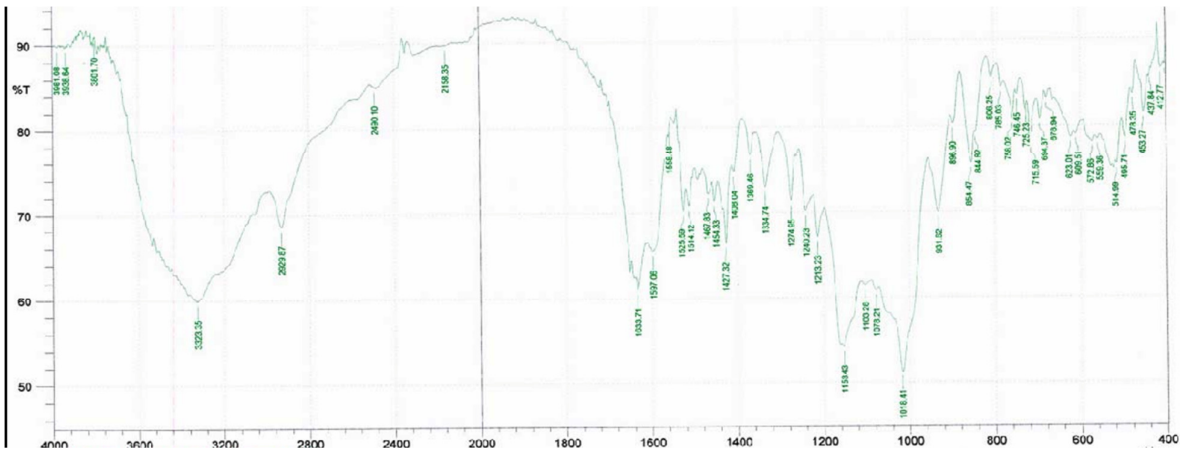

Fig .3. FTIR of Sitagliptin optimized formulation

Table.3. Physical Characteristics of powder blend of drug and Excipients

Formulation code	BD(g/cc)	TD(g/cc)	CI	HR	AR(θ)
M1	0.322 ± 0.03	0.38 ± 0.024	15.26 ± 0.6	1.1	21.12
M2	0.354 ± 0.03	0.385 ± 0.022	.05 ± 0.3	1.11	22.4 ± 1.12
M3	0.328 ± 0.02 0.	414 ± 0.019	20.77 ± 0.93	1.23	24.1 ± 1.13
M4	0.355 ± 0.04	0.425 ± 0.014	16.44 ± 1.05	1.3	24.2 ± 1.25
M5	0.328 ± 0.03	0.382 ± 0.018	14.13 ± 0.61	1.52	22.8 ± 1.06
M6	0.358 ± 0.06	0.41 ± 0.022	12.68 ± 1.25	1.13	23.4 ± 1.16

*Bulk density, Tapped density, Carr's Index, Hausner Ratio, Angle of repose

Table.4. Post compression parameters of Sitagliptin floating tablet

Formulation code	Weight Variation(mg)	Thickness(mm)	Hardness (kg/cm2)	Friability (%)
M1	195±2.37	3.28±0.20	3.7±0.54	0.52±0.41
M2	197±1.12	3.33±0.22	3.5±0.75	0.37±0.42
M3	192±2.76	3.28±0.17	3.6±0.17	0.40±0.38
M4	196±2.09	3.16±0.05	3.4±0.25	0.46±0.36
M5	197±2.19	3.84±0.17	3.9 ±0.44	0.32±0.25
M6	196±1.89	3.92±0.25	3.8±0.31	0.6±0.31

Table.5 : Floating study of Sitagliptin floating tablet

Formulation code	Floating lag time	total floating time (hrs)
M1	52 sec	6.3
M2	45 sec	8.3
M3	48 sec	11
M4	32 sec	10
M5	30 sec	12
M6	36 sec	11

Table.6. Result of Dissolution data of formulation M1-M6

	M1	M2	M3	M4	M5	M6
1	21	18	16	20	16	13
2	35	33	33	35	32	28
3	42	41	38	42	40	36
4	55	52	50	52	52	50
5	69	65	63	67	66	62
6	83	74	76	76	73	68
7	94	83	80	88	82	75
8		97	90	99	94	89

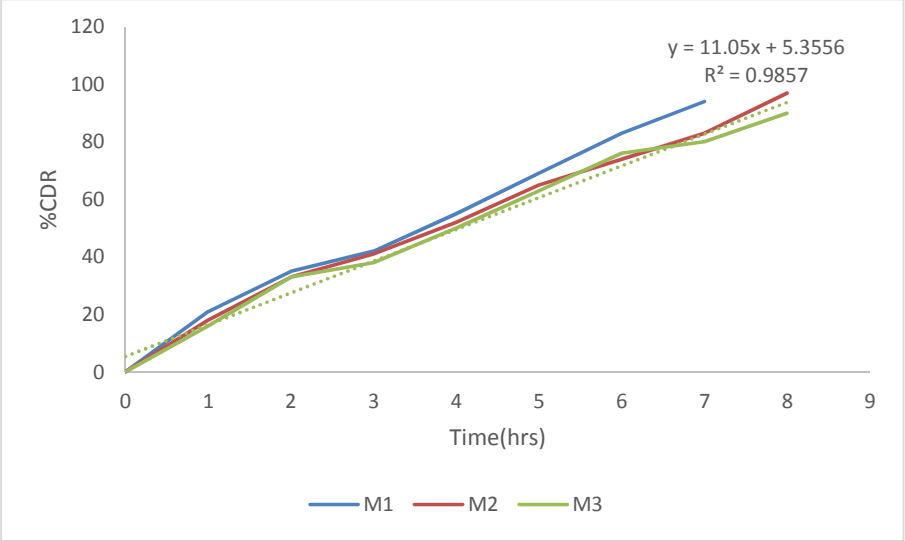

Figure 4: Dissoulation graph for M1 – M3

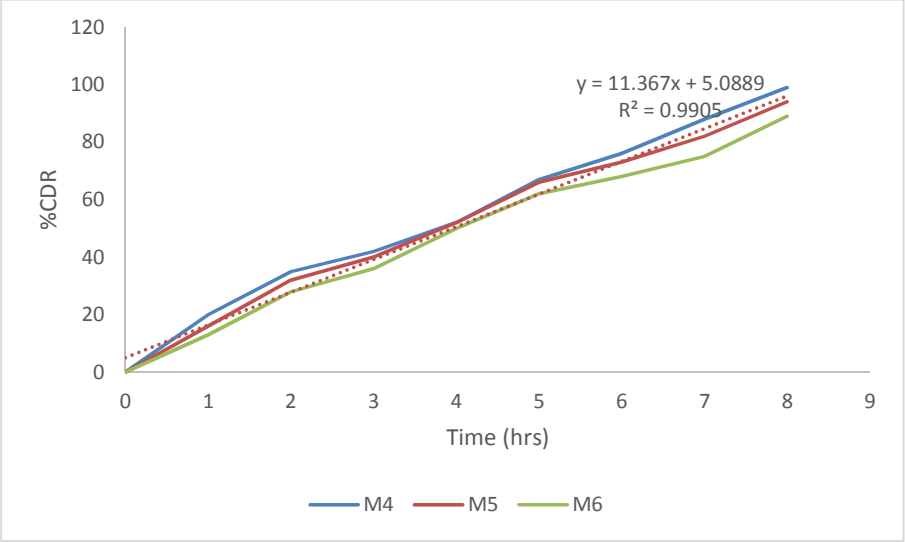

Figure 5: Dissolution graphs for M4-M6

Conclusion

The study successfully developed floating tablets of Sitagliptin, a crucial antidiabetic medication, employing a gastroretentive drug delivery system. The tablets exhibited favorable physicochemical properties and micromeritics characteristics, ensuring their suitability for prolonged gastric residence. Compatibility studies via FTIR spectroscopy confirmed the compatibility of excipients with Sitagliptin. Pre-compression evaluations demonstrated consistent flow properties across formulations. Post-compression analysis revealed satisfactory parameters such as weight variation, thickness, hardness, and friability. Notably, formulation M5 emerged as the most promising candidate, displaying a floating lag time of 30 seconds and a prolonged floating duration of 12 hours. Moreover, M5 exhibited robust in vitro drug release profiles, ensuring sustained release over 8 hours. These findings underscore the potential of M5 as an effective gastroretentive delivery system for Sitagliptin, offering enhanced patient compliance and therapeutic efficacy. Overall, the developed formulation presents a promising approach for optimizing the treatment of diabetes mellitus type II, addressing the need for sustained drug release and improved patient adherence in diabetes management

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