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DEVELOPMENT AND OPTIMIZATION OF VILDAGLIPTIN LOADED FLOATING MICROSPHERES USING CENTRAL COMPOSITE DESIGN: IN VITRO AND IN VIVO EVALUATION

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ABSTRACT

The aim of the study was the development and optimization of vildagliptin floating microspheres using a central composite design. The selected independent variables were Chitosan, Eudragit RL100, and Sodium lauryl sulphate. The selected dependent variables were mean particle size, entrapment effectiveness, and drug release within 12 h. Further, the microspheres were categorized for particle size, micrometric study, entrapment effectiveness, in vitro drug discharge, kinetic studies for drug release, SEM, DSC, FTIR of the optimized formulation. *In-vivo* floating capability (X-ray) study and *in-vivo* antidiabetic action were performed using the Streptozotocin model. The vildagliptin microspheres were found free-flowing with excellent results for mean particle size (20.22 to 32.23 μm) and the entrapment efficiency (62.02±2.38 to 89.02±1.72%), Percentage yield (63.12 to 92.89%), and buoyancy studies (52.53 to 94.67%). SEM has shown a spherical organization of microspheres with soft surface morphology. Formulation code F7 was found to be the finest formulation as it releases vildagliptin 90.54±1.21**%** in a sustained manner. The results for *in vivo* antidiabetic activity and *in vivo* gastric retention for 12 hours were also found very significant. As per results obtained from *in vitro* and *in vivo* studies, floating microspheres of vildagliptin may prove to be a potential contender for secure and efficient sustained drug release over an absolute phase of time which can decrease dosing frequency.

Keywords
Vildagliptin, microspheres, central composite design, *in vitro* and *in vivo* studies

INTRODUCTION

Significant attention has now been given to the oral dosage type able to extended retention in the stomach to expand the release of drugs for a longer period. One of the significant factors influencing the bioavailability of drugs in pharmaceutical dosage forms is gastric residence time (GRT) [1]. Partial drug release from the delivery system above the absorption region (stomach and duodenum of small intestine), will result in changeable and small gastric emptying time and thereby, obliterates the efficiency of administered dose. By prolonging GRT via gastro-retentive dosage form such as the floating drug delivery system (FDDS), drug bioavailability can be adequately improved [2]. The bulk density of FDDS is minor than gastric fluids, so they remain floating in the stomach for a long phase of time with having no any effects on the rate of gastric emptying. The discharge of drug is decreases when the device is floating in the fluids. The residual organization is drained from the stomach after the drug is released. This results in improved GRT and better regulation of plasma drug concentration fluctuations [3]. Both single and multiple systems have been built in the floating dosage form. Multiple unit dosage form can be an appealing another to single unit form as it has been shown that inter and intra drug absorption variabilities have been reduced as well as the risk of dose addition has been reduced.

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Targeted dosage formulations of the gastrointestinal tract are organized to liberate the drug at the gastrointestinal site [4]. Tiny spherical particles with a diameter of between 1 μm and 1000 μm are microspheres. They are free flowing spherical particles containing proteins that are biodegradable in nature, or synthetic polymers. There are two types of microspheres, micromatrices and microcapsules, defined as the trapped material of microcapsules is separately surrounded by separate capsule walls. Sometimes these are referred as microparticles. By using various natural and synthetic materials microspheres can be manufactured. To improve bioavailability of conventional drugs and minimizing side effects microsphere play an important role [5].

Vildagliptin is a novel dual-type dipeptidyl peptidase-4 (DPP 4) inhibitor, efficiently regulate endocrine levels in both hypoglycemia and hyperglycemia, and can be used both as monotherapy and in grouping treatment for the cure of type 2 diabetes mellitus (T2DM) [6]. VLG is not efficient in providing control over drug delivery with usual oral dosage forms because of short elimination half-life of 1.6 to 2.5 hand rapid metabolism, causing significant variations of drug levels in plasma. It is suggested that patients having (T2DM) should conform precisely to the dosing time and that vildagliptin should be taken twice daily 50 mg dose [7].

MATERIALS AND METHOD

Material

Vildagliptin API (B.no. VNFP1903) was supplied by Zydus health care private limited Ahemdabad, Gujrat, India as agift sample. Acetic acid were purchased from Loba Chemie, Mumbai, India. DSC was used as DSC-60 (SHIMADZU) with thermal analyzer (TA Instrument Trios V4.1). IAEC approved Protocol No: CCP/IAEC/Feb2021/17.

Methods

Preparation of Microspheres

The microspheres were prepared according to the concentration of different batches given below in table 1. Both polymers i.e. Chitosan and Eudragit RL 100 were mixed in 50 ml Acetic Acid (1%v/v). Then drug (100mg) was added to the above solution. After that the solution was stirred at 200rpm for 1 hr at temperature 25-30°C, this becomes first solution. On the other hand, second solution was prepared by dissolving sodium lauryl sulphate in water. Further, Syringe having diameter 0.5mm was used to add first solution dropwise to the second from a falling distance of 5cm and microspheres started to form. Finally, Resulting microspheres were filtered, collected and air dried for 48 hours at room temperature [8].

Table 1: Formulation Composition by Central Composite Design

Batch No.	X_1 (Chitosan)(mg)	X_2 (Eudragit RL 100)(mg)	X_3 (Sodium Lauryl Sulphate) (%w/w)
F1	-1 (100)	-1 (100)	-1 (1)
F2	-1 (100)	-1 (100)	+1 (3)
F3	-1 (100)	+1 (300)	-1 (1)
F4	-1 (100)	+1 (300)	+1 (3)
F5	+1 (200)	-1 (100)	-1 (1)
F6	+1 (200)	-1 (100)	+1 (3)
F7	+1 (200)	+1 (300)	-1 (1)

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F8	+1 (200)	+1 (300)	+1 (3)
F9	-1.682 (65.91)	0 (200)	0 (2)
F10	+1.682 (234.09)	0 (200)	0 (2)
F11	0 (150)	-1.682 (31.8207)	0 (2)
F12	0 (150)	+1.682 (368.179)	0 (2)
F13	0 (150)	0 (200)	-1.682 (0.31)
F14	0 (150)	0 (200)	1.682 (3.68)
F15	0 (150)	0 (200)	0 (2)
F16	0 (150)	0 (200)	0 (2)
F17	0 (150)	0 (200)	0 (2)
F18	0 (150)	0 (200)	0 (2)
F19	0 (150)	0 (200)	0 (2)
F20	0 (150)	0 (200)	0 (2)

EVALUATION OF MICROSPHERES

Entrapment Efficiency

Evaluation of entrapment efficiency in floating microspheres was carried out by dissolving the weighed quantity of compressed microspheres in necessary amount of 0.1 N HCl and analyzed spectrophotometrically at wavelength 210nm. Each batch was examined for drug quantity in a triplicate manner. The entrapment effectiveness of floating microspheres is calculated by dividing the real drug amount by the theoretical drug amount of microspheres [9].

Percentage Yield

The prepared microspheres were weighed accurately. The weighed quantity of microspheres was divided by the entire quantity of all the excipients and drugs used in the formulation of the microspheres, giving the floating microspheres a total percentage yield [10].

Buoyancy Studies

Microspheres were spread over the 900 mL of 0.1 N HCl placed in USP dissolution apparatus type II. The medium was stirred at 100 rpm at 37±0.5°C. After definite intervals of time, all the two fractions of microspheres (floating and settled microspheres) are collected and buoyancy of the floating microspheres was calculated [10].

Micromeritics Studies

Optical Microscopy

All microspheres were analysed using a visual microscope (OLYMPUS CH 20i) with customized magnus pro 3.0 software and Olympus master by means of a camera using an amount of dried microspheres suspended in glycerin with reference to their size and shape. The visual microscope randomly calculated the diameters of particle more than 100 microspheres. The average particle dimension of the microspheres was stated as the volume surface diameter.

Bulk Density (BD) and Tapped Density (TD)

2 g of granules blend was introduced to a measuring cylinder of 100 ml. The cylinder was tapped 100 times and the tapped volume of packing was recorded [11].

Angle of Repose

This is the angle of a pile of microspheres blending between the horizontal plane and the surface. By using the funnel process, it was calculated. In the funnel, the perfectly weighed granule blend is collected. Adjusted to the optimum cone height (h) and microspheres blend, the altitude of the funnel was freely poured onto the surface through the funnel. Then by measuring the radius of the

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heap (r), angle of repose was calculated [11].Then Carr's Compressibility Index and Hausner's Ratio were calculated [12].

In vitro drug release

Using the USP dissolution paddle assembly the drug release from formulated microspheres was examined. Initially, the dissolution media was 900 mL of 0.1 N HCl, the paddle with 100 rpm velocity, and 37 °C temperature. About 20 mg of corresponding Vildagliptin microspheres were taken from every group into a size 2 capsule shell and transferred to each dissolution basket. The dissolution process was done over a period of 12 hours and a 10 mL dissolution sample was withdrawn at fixed intervals of time and replaced with the similar test medium volume in order to preserve submerged conditions. Each 10 ml dissolution sample was compensated with a new 10 mL of 0.1 N HCl each time. With the help of a 10 mL syringe, dissolution samples were removed and kept back in the test tube. Dilute thewithdrawn samples, filtered through a 0.45µ membrane filter where appropriate, and spectrophotometrically assayed at 210 nm. Data of dissolution for all the samples were recorded in triplicate [4].

Optimization of Formulation using Design Expert Software

The formulation variables were selected as; Chitosan, Eudragit RL100 and Sodium lauryl sulphate at three levels -1, 0, and +1. The responses selected for this formulation are: Particles size, Drug entrapment efficiency and Drug release.

***In vivo* gastric retention studies**

In vivo gastric retention tests on Albino Rabbit have been conducted to validate the gastric retention of the dosage type. Three adult albino rabbits with a body weight of 150-200gm were chosen. The animals were easy to maintain sufficient gastric fluid content overnight with free access to water. By reformulating batch F7 with barium sulphate instead of a drug, the dosage form for the in vivo analysis was prepared. As a radio contrast agent, barium sulphate was used. An X-ray machine was used to take radiographs of the abdomen at a pre-determined time interval [13].

***In vivo* Antidiabetic Activity**

Experimental Animals: First of all (about 150 to 200 gm) wistar albino rats from animal house were taken and then were set aside in an area with a 12-hour day-night period at a temperature of 22 ° C and humidity of 45-64 percent. The rats were fed on pellets with free intake to distilled water during the investigational analysis.

Induction of Experimental Diabetes

Rats were converted into diabetic ones via a single intraperitoneal injection of freshly formed Streptozotocin (STZ-65 mg/kg body weight) in citrate buffer (pH 4.5) and concentration 0.1 M with a volume of 1 mL/kg body weight. Standard rats received 1ml citrate buffer as vehicle. Blood glucose level in rats following all night fasting were estimated after 48 hours of Streptozotocin administration. Blood glucose rats ranging from 200 to 300 mg/dL were collected as diabetic and used for the experiments [14].

Drug and Chemical: Streptozotocin, Pure Drug: Vildagliptin, Batch F7 as optimized formulation.

Experimental Design: The rats were classified into 4 groups with 6 animals in each group as follows.

Group I (Negative Control): Saline treatment of normal rats daily.

Group II (Positive Control): Animals were treated with a particular dose of Streptozotocin (65 mg/kg) by the intraperitoneal route to induce diabetes.

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Group III (Pure Vildagliptin): Treatment of diabetic rats with 2.5 mg/kg body weight of pure Vildagliptin.
Group IV (Formulation F7): Treatment of diabetic rats with 2.5 mg/kg body weight of Vildagliptin containing microsphere.
Blood collection from rats: The rats were sacrificed by cervical dislocation after mild chloroform anaesthesia following the experimental course of therapy. On decapitation, blood is extracted and serum is separated by centrifugation (for 20 min at 2000 rpm).
Estimation of serum or plasma biochemical parameters: Serum glucose, cholesterol, triglycerides, high density lipoprotein, total protein, urea, bilirubin and creatinine were assayed by the use of diagnostic reagent kit.

Statistical Analysis

Results are represented as mean±SD. One-way analysis of variance (ANOVA) followed by Bonferroni Post hoc test was done. Statistical significant values were considered as p-value of less than 0.05.

Comparative Study

Optimized formulation v/s conventional formulation:

Comparative study was done in between the optimized formulation (F7) and marketed formulation (MF) of Vildagliptin tablets [Galvas® (50mg); Norvartis]. Dissolution profile was carried out for both the two formulation by using same procedure as described above.

RESULT AND DISCUSSION

The prepared microspheres were evaluated by using various parameters and as a result all batches were found spherical in shape. Further their results are described below:

Percentage Yield, Buoyancy Studies and Entrapment Efficiency

Percentage yield was found in the range of 63.12 to 92.89 and buoyancy studies were ranged from 52.53 to 94.67% (table 2). The entrapment efficiency of the prepared microspheres ranged from 62.02±2.38 to 89.02±1.72% (table 3). In this way the results obtained indicates good efficiency. The p value and ANOVA of regression is given in table 4.

Optical Microscopy and Micromeritics Studies

All the formed microspheres were found spherical in shapes with excellent flow properties. The results for micromeritics studies i.e. bulk density, tapped density, angle of repose and hausner's ratio were found within the range. The obtained results by optical microscopy are given in table 2. The mean particle size was ranged from 20.22 to 32.23 μm (Table 3).

Table 2: Percentage Yield and Buoyancy Studies and Shapes of all batches

Formulation Code	Percentage Yield (%)	Buoyancy (%)	Shape
F1	78.63	81.28	Spherical
F2	78.67	70.32	Spherical
F3	86.45	76.55	Spherical
F4	79.79	76.36	Spherical
F5	82.28	52.53	Spherical
F6	87.43	66.32	Spherical
F7	92.89	94.67	Spherical
F8	82.40	56.87	Spherical

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F9	80.49	67.88	Spherical
F10	79.68	77.35	Spherical
F11	74.34	78.55	Spherical
F12	65.78	69.93	Spherical
F13	63.12	80.54	Spherical
F14	74.63	90.27	Spherical
F15	77.66	80.33	Spherical
F16	77.63	80.36	Spherical
F17	77.62	80.34	Spherical
F18	77.66	80.55	Spherical
F19	77.65	80.32	Spherical
F20	77.69	80.28	Spherical

Table 3: Responses of dependent variables: mean particle size, entrapment efficiency and drug release

Formulation Code	Mean Particle Size (µm)	Entrapment Efficiency (%)	*In-vitro* Drug Release (%)
F1	22.62±0.13	80.02±3.73	78.42±1.14
F2	29.47±0.21	83.12±2.12	80.54±1.13
F3	32.23±0.74	75.22±1.72	82.02±1.13
F4	21.43±0.65	76.42±1.55	77.21±2.03
F5	28.43±0.55	70.02±3.72	78.41±2.16
F6	23.56±0.84	82.05±6.32	79.92±2.61
F7	20.22±0.11	84.32±2.76	90.54±1.21
F8	23.78±0.74	89.02±1.72	86.67±1.23
F9	27.89±0.35	66.02±2.13	76.67±1.87
F10	24.87±0.71	79.02±1.64	80.92±2.31
F11	29.66±0.42	64.02±2.79	68.23±2.88
F12	26.38±0.32	62.02±2.38	87.71±1.76
F13	25.88±0.89	73.02±1.76	89.21±2.08
F14	30.62±0.92	80.02±2.72	85.52±1.98
F15	31.47±0.77	73.12±2.15	78.45±2.31
F16	31.43±0.64	73.22±2.15	79.25±2.12
F17	31.45±0.67	73.22±2.15	79.59±2.33
F18	31.46±0.70	73.15±2.15	79.95±2.42
F19	31.56±0.66s	73.14±2.15	78.58±2.45
F20	31.52±0.61	73.13±2.15	79.44±2.61

Standard Deviation (±) where, n=3

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Table 4: ANOVA of the Regression (%CDR)

	Degree of freedom	Sum of squares	Mean square	F	p-value significance
Total	19	416.61	-	-	-
Residual	16	173.08	10.82	-	-
Regression	3	243.53	81.18	7.50	0.0024*

p value less than 0.050 indicates model terms are significant

***In vitro* drug release**

The release of drug from the microspheres was varied in the range of 68.23±2.88% to 90.54±1.21% in 12 h study (Table 4) due to result of self-governing factors in combination. Graphs of in vitro drug release data are plotted between % Cumulative Drug Release and time are shown in fig 1 for all batches.

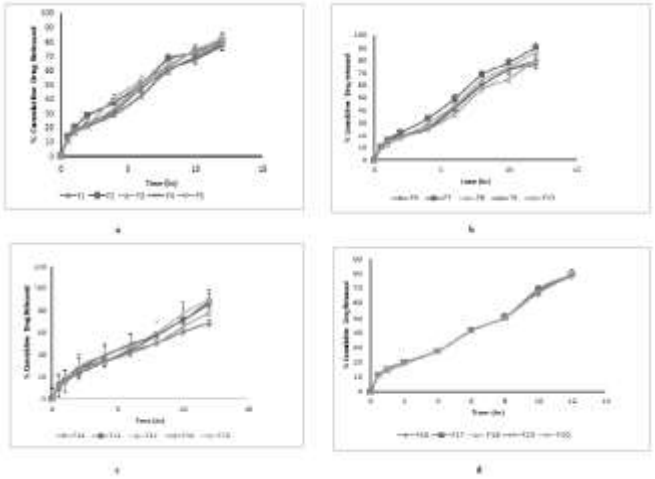

Fig 1: *In-vitro* Drug Release Profile of Batch F1-F5 (a), Batch F6-F10 (b), Batch F11-F15 (c) and Batch F16-F20 (d)

Optimization of Formulation using Design Expert Software

By using the design expert the formulations were optimized. 3D response surface plots are shown in fig 2 as for Particle Size fig 2(a), Entrapment Efficiency fig 2(b) and %CDR fig 2(c). 2D contour plots are shown in fig 3 as for Particle Size fig 3(a), Entrapment Efficiency fig 3(b) and %CDR fig 3(c).

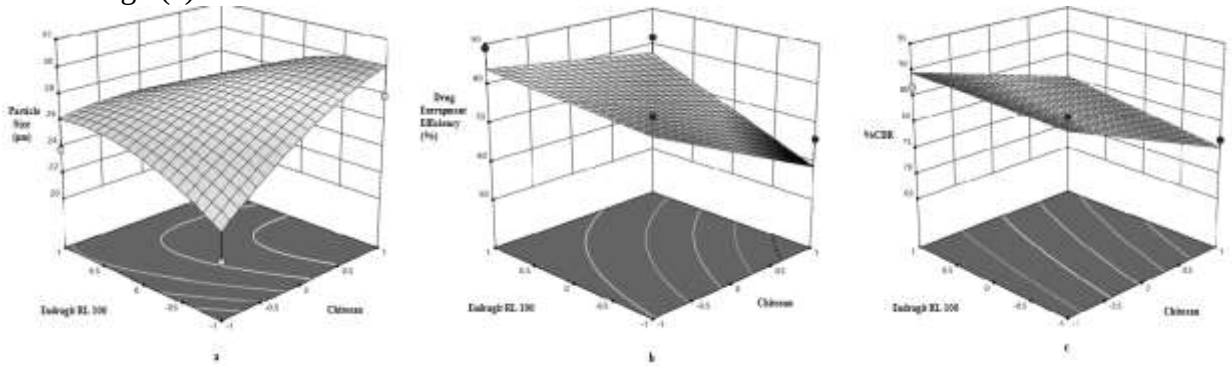

Fig 2: 3D Surface Model Graph for Particle Size (a), Entrapment Efficiency (b) and %CDR (c)

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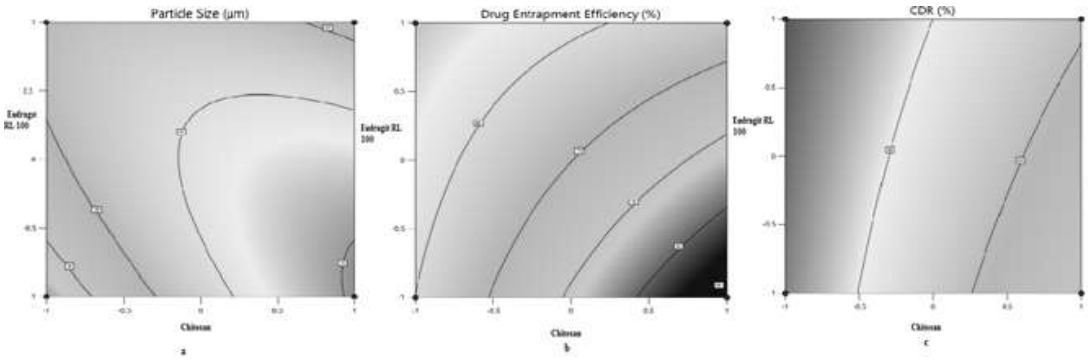

Fig 3: Contour Model Graph for Particle Size (a), Entrapment Efficiency (b) and %CDR (c)

$$Y = 83.86 + 1.14\,A + 1.49B - 1.47\,C + 1.76\,AB - 0.98\,AC - 0.66\,BC + 1.29\,A^2 - 0.44\,B^2 - 0.40\,C^2$$

Where, Y is % CDR, A is concentration of Chitosan, B is concentration of Eudragit RL 100 and C is concentration of Sodium Lauryl Sulphate.
Effect of coefficient for both polymers is positive while for the SLS it indicates negative effect. Results obtained from ANOVA are given in table 4.

Selection of Optimized Formulation

Based on best results obtained from various evaluation parameters i.e. entrapment efficiency (84.32±2.76%), % yield (92.89%) and buoyancy studies (94.67%), excellent micromeritics properties i.e. spherical and smallest particle size (20.22µm), highest cumulative drug release (90.54±1.21) over a period of 12 hours. Thus formulation code F7 was selected as optimized batch. Then SEM, DSC and FTIR were also performed for the optimized formulation to determine size, melting point and confirm its functional structure. The FTIR spectra were found in between 4000 and 400 cm−1 and the resolution was 2 cm−1. SEM is shown in figure 4 while DSC and FTIR spectra of pure drug compared with optimized batch are shown in figure 5 and 6 respectively. The DSC thermogram of optimized formulation showed their peak of endothermic at 167.68 °C corresponds to melting point.

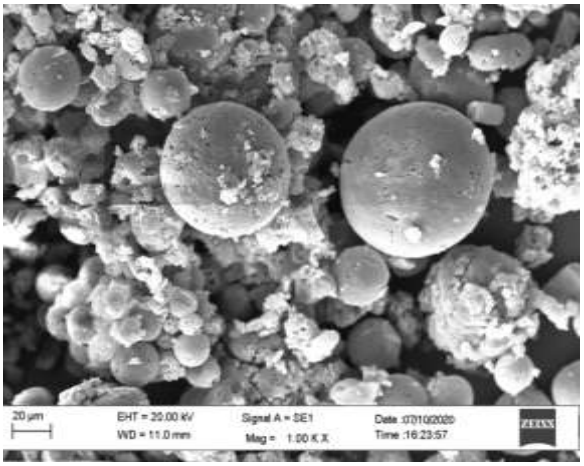

Fig 4: SEM of Optimized Formulation

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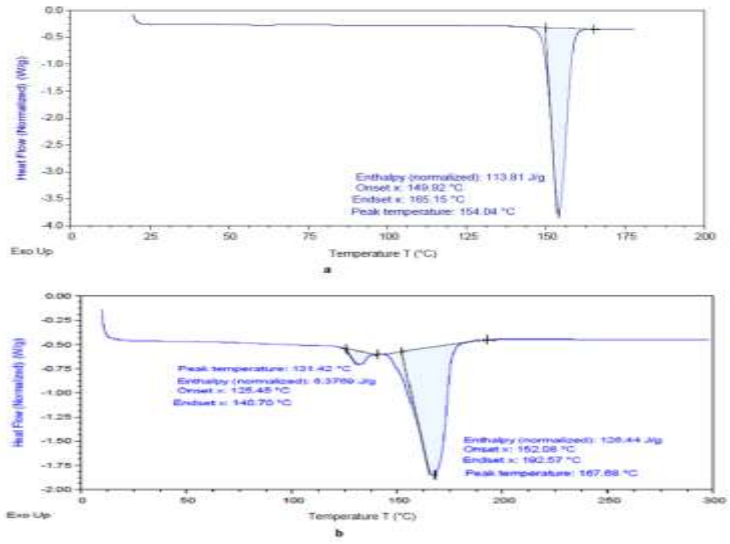

Fig 5: Differential Scanning Calorimetry (DSC) of Pure Drug (a) and Optimized formulation (b)

Peaks obtained at 2919.20 cm-1 showed C-H stretching, at 3300-2500 cm-1 showed OH stretching , at 1653.82 cm-1 indicated C=O stretching and at 1220 cm-1 confirmed C-N stretching.

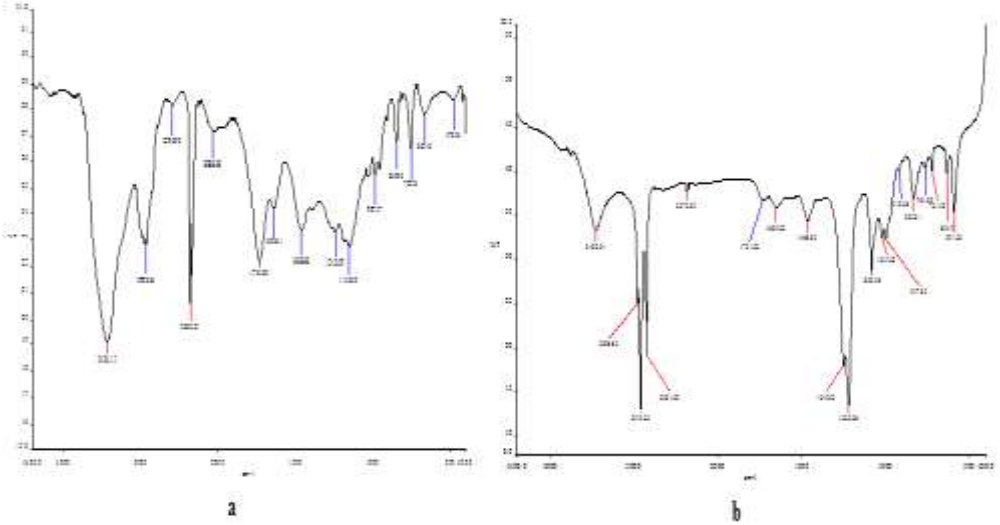

Fig 6: Fourier Transform Infrared (FTIR) Spectroscopy of Pure Drug (a) and Optimized formulation (b)

Drug Release Kinetic Studies

The release data were fitted to zero order, first order, Korsmeyer-peppas model and Higuchi equation to know the mechanism of drug release from the microspheres. The closure data was therefore applied to the well-known exponential equation (Higuchi equation), also used to explain the polymeric system's drug release behaviour [15,16]. Plots for zero order, first order, Higuchi and Korsmeyer-peppas models are shown in fig 7 (a, b, c, d) respectively. Value of regression

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coefficient (R2) for different plots were found as 0.9627, 0.8135, 0.9801, 0.6301 for zero order, first order, Higuchi and Korsmeyer-peppas models respectively.
The release profile of the optimized batch F7, fitted best to the Higuchi model (R^2= 0.9801). Thus, gastro retentive drug delivery system of vildagliptin microspheres is best explained by the Higuchi model.

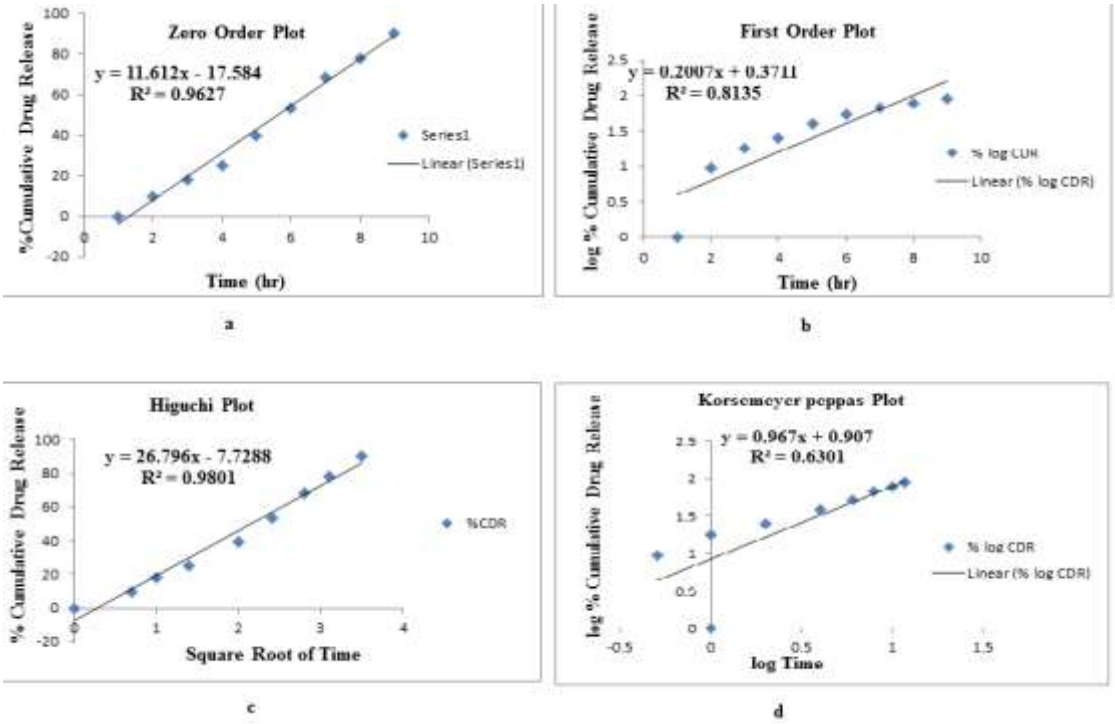

Fig 7: Drug Release Kinetic Plots for Zero Order (a), First Order (b), Higuchi (c) and Korsmeyer-peppas Models (d)

***In vivo* gastric retention studies**

The optimized batch F7 was observed for the gastric retention of the formulation in the stomach of albino rabbit by X-ray imaging [13] (Fig 8). The buoyancy of the formulation was observed for 12 hours. It was observed that the formulation was in floating condition till 12 hours of the study.

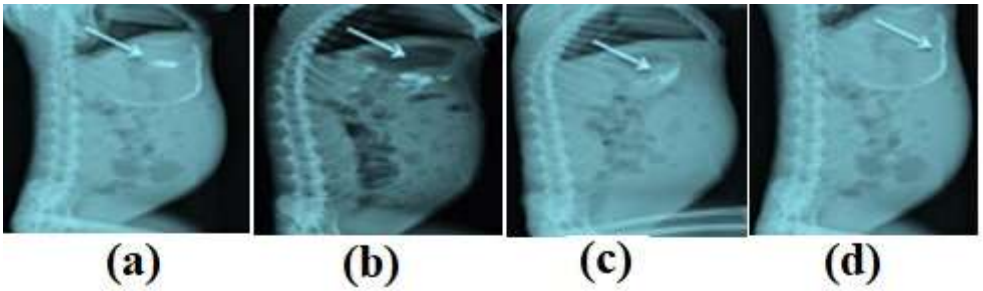

Fig 8: Radiographic images showing the presence of BaSO4 loaded floating microspheres in the stomach at different time intervals. Images were taken after a: 0 h, b: 4 h, c: 8 h, d: 12 h.

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Study of In-Vivo Anti-hyperglycemic on Wistar Albino Rats

Streptozotocin in rats was significantly capable of inducing diabetics [14] (as shown in table 5). On the other hand, for up to 4 hours, the blood glucose level decreased irregularly and then the blood glucose level rose to the maximum, so the drug was not released on a continuous basis. It may be because, here, the activity of DPP-4 was rapidly inhibited by Vildagliptin, which for a short time increased the fasting and postprandial endogenous levels of GLP-1 (glucagon-like peptide1) and GIP incretin hormones and rapidly decreased blood glucose levels.

Table 5: Average reduction in glucose level (mg/dL) in negative control, positive control, pure drug Vildagliptin and formulation F7

Time (hours)	Blood glucose level (mg/dL)			
	Negative control (group I)	Positive control (group II)	Pure drug (group III)	Formulation F7 (group IV)
0	85 ± 4.291	283.5± 3.18	289.7± 2.67	291.2 ± 5.22
1	85 ± 4.291	316.2± 3.18*	233.5 ± 2.67$^{\#}$	220.4± 5.22$^{\#}$
2	85 ± 4.291	335.7 ± 3.18*	168.2 ± 2.67$^{\#}$	211.3 ± 5.22$^{\#}$
3	85 ± 4.291	344.2 ± 3.18*	128.4 ± 2.67$^{\#}$	205.6 ± 5.22$^{\#}$
4	85 ± 4.291	353.5 ± 3.18*	109.8 ± 2.67$^{\#}$	182.3 ± 5.22$^{\#}$
5	85 ± 4.291	369.3 ± 3.18*	122.4± 2.67$^{\#}$	148.6 ± 5.22$^{\#}$
6	85 ± 4.291	370.4 ± 3.18*	145.9 ± 2.67$^{\#}$	113.5 ± 5.22$^{\#}$
7	85 ± 4.291	388.6 ± 3.18*	168.1 ± 2.67$^{\#}$	102.7 ± 5.22$^{\#}$
8	85 ± 4.291	392.5 ± 3.18*	189.2± 2.67$^{\#}$	97.8± 5.22$^{\#}$
12	85 ± 4.291	400.4± 3.18*	230.3± 2.67$^{\#}$	91.4 ± 5.22$^{\#}$
24	85 ± 4.291	412.7 ± 3.18*	290.6± 2.67$^{\#}$	190.6 ± 5.22$^{\#}$
48	85 ± 4.291	428.9 ± 3.18*	320.5± 2.67$^{\#}$	230.5± 5.22$^{\#}$

All value are Mean±SD (n=6). $^{*}P<0.05$ comparing with Negative control, $^{\#}P<0.05$ comparing with Positive control (one way ANOVA followed by Bonferroni Post Hoc Test).

It can therefore be inferred from the findings that drug retardant polymers and their amount significantly affect every assessment parameters. Therefore, prepared vildagliptin polymeric microspheres may be shown to be a possible candidate for safe and successful sustained delivery of drugs from microspheres for the treatment of type II diabetes. Effect of drug and formulation on lipid profile is given in table 6.

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Table 6: Effect of drug and formulation on lipid profile of control and experimental groups

Groups/Treatment	Total Cholesterol (mg/dL)	Triglycerides (mg/dL)	HDL- cholesterol (mg/dL)
Negative control (group I)	50.28 ± 3.8	70.42 ± 5.16	37.32 ± 2.9
Positive control (group II)	194.73 ± 7.6*	163.52 ± 4.71*	58.23 ± 2.2*
Pure drug (group III)	32.32 ± 2.4#	90.32 ± 2.35#	40.24 ± 2.2#
Formulation F7 (group IV)	51.12 ± 1.4#	72.25 ± 3.25#	38.23 ± 1.5#

All value are Mean±SD (n=6). *P<0.05 comparing with Negative control, #P<0.05 comparing with Positive control (one way ANOVA followed by Bonferroni Post Hoc Test).

COMPARATIVE STUDY

Comparative study was performed between the optimized formulation (F7) and marketed formulation (MF) of Vildagliptin tablets [Galvas® (50mg); Norvartis]. Comparative data for these two formulations is shown in Table 7.

Table 7: Comparative Study

Time (h)	MF (%CDR)	F7 (%CDR)
0	0	0
0.5	60.23± 1.98	9.55± 1.67
1	91.75± 1.84	17.99± 1.83
2	99.58± 0.22	25.25± 1.54
4		39.61± 1.63
6		53.48± 1.75
8		68.66± 1.91
10		78.22± 1.33
12		90.54± 1.12

The result revealed that in comparison to the marketed product, the optimized formulation F7 has better control over release rate of drug. Drug release in marketed product was found the 99.58% in 2 hours whereas the drug release in optimized formulation F7 was found 90.54 % in 12 hrs. Thus the optimized formulation was found better controlled drug release over 12 hrs, which was found for longer time than the marketed formulation. The comparative drug release of these formulations is shown Figure 9.

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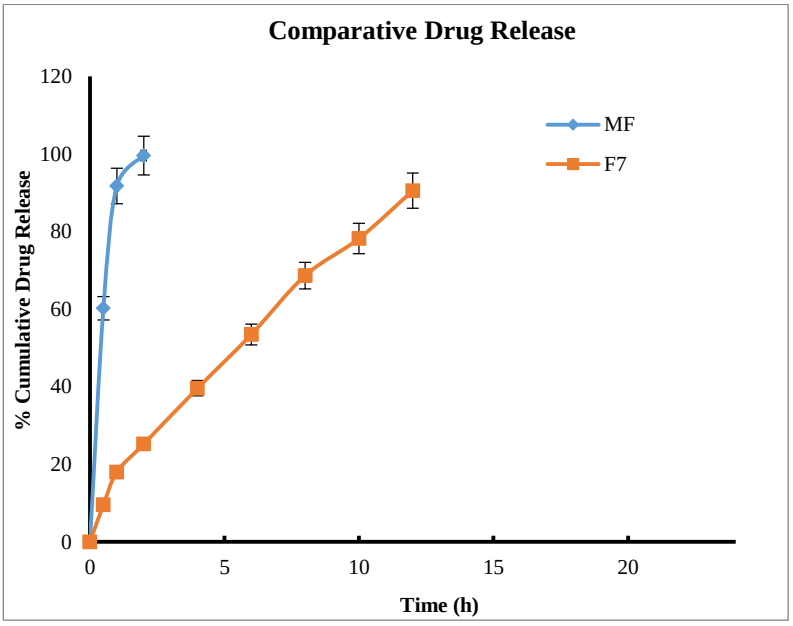

Figure 9: **Comparative Release Profile of MF (Galvas®) and Optimized Batch F7**

CONCLUSION

The percentage release was maximum at high value of Chitosan, high level of Eudragit RL 100 and low levels of Sodium Lauryl Sulphate. While initially the drug release was slow but as time rises the %CDR increases due to hydrophilicity of polymer. However, high amounts of both the polymers are required for increase in %CDR. The combination of Chitosan (high) and Eudragit (high) with Sodium Lauryl Sulphate (low) was found to achieve optimum in vitro release and buoyancy. The drug release at 12 hr was more than 90%. Hence from in vitro and in vivo results it can be concluded that a floating based system of Vildagliptin could be promising Gastro-retentive drug delivery system with sustained release characteristics.

Compliance with Ethical Standards

Conflict of Interest

The authors declare that they have no conflict of interest.

Ethical Approval

The in vivo study was approved by Institutional Animal Ethics Committee, Chandigarh College of Pharmacy, Chandigarh Group of Colleges, Landran, Mohali, Chandigarh, Haryana (Protocol No: CCP/IAEC/Feb2021/17).

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