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FORMULATION *IN-VITRO* CHARACTERIZATION AND OPTIMIZATION OF CONTROLLED RELEASE OSMOTIC TABLET OF SITAGLIPTINE USING 3^2 FULL FACTORIAL DESIGN

K.Shivani*, Vasudha Bakshi, B.Nirosha, Nagilla Swetha, Dibyalochan Mohanty

Department of Pharmaceutics, Center for Nanomedicine, School of Pharmacy, Anurag Group of Institutions, Hyderabad, Pin-500088, INDIA.

Corresponding author E-mail:* dibyalochan.mohanty@gmail.com

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ABSTRACT

The Present investigation deals with formulation evaluation optimization of controlled release osmotic tablets using 3^2 full factorial experimental design. Nine formulation were formulated according to factorial design,Osmotic agent sodium chloride(X1) and SLS(X2) were considered as independent variables. Drug Release rate at 2 h, 6h, 12h and release exponent (n) were taken as responses. The increase in concentration of pore former and osmotic agent after a limit, changes the release from zero order to Higuchi based release. The optimized formulation follows non-Fickian release mechanism. The FT-IR and DSC studies revealed that no physicochemical interaction between excipients and drug. The influence of pH and agitation intensity on the release of drug was studied and the release mechanism was through osmosis. Stability studies revealed that optimized formulation was stable. The observed independent variables were found to be very close to predicted values of optimized formulation which demonstrates the feasibility of the optimization procedure in successful development of porous osmotic pump tablets containing Sitagliptine as model drug by using sodium chloride (30mg) as osmotic agent, sodium lauryl sulphate (30mg) as pore former, cellulose acetate (2%) as coating agent, and control membrane permeability. Batch F9 was selected as optimized batch. Stability studies also revealed that optimized formulation is stable.

INTRODUCTION

Oral route is a convenient route for the administration of various drugs because of low cost and ease of administration to the patients. But conventional drug delivery system does not control the release of drug and provides immediate release of drug. The development of novel drug delivery system (NDDS). Among various designs of NDDS available in the market per oral controlled release system provides improved patient compliance, convenience and reduction in fluctuation in a steady state plasma level. The release of drug from osmotic system is independent of presence and absence of food, pH of gastrointestinal (GI) tract, GI motility and hydrodynamic conditions of body due to rate controlling semi permeable membrane. In ODDS the drug dose and dosing interval are optimized to maintain drug concentration within the therapeutic window. ODDS delivers the drug at predetermined zero

order rate for a prolonged time period. So it is used as the standard dosage form for constant drug delivery. ODDS provides a uniform concentration of drug at the site of absorption and thus after absorption allows maintenance of plasma concentration within therapeutic range which minimizes side effects and reduces the frequency of administration.

Sitagliptin is a DPP-4 inhibitor, which is believed to exert its actions in patients with type 2 diabetes by slowing the inactivation of incretin hormones. Concentrations of the active intact hormones are increased by JANUVIA, thereby increasing and prolonging the action of these hormones. Incretin hormones, including glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), are released by the intestine throughout the day, and levels are increased in response to a meal.

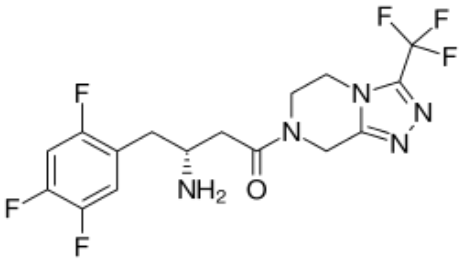


Fig:1. Structure of Sitagliptine

EXPERIMENTAL:

ANALYTICAL METHOD DEVELOPMENT FOR SITAGLIPTINE

Calculation of λmax for sitagliptine in 0.1 N HCl

UV visible spectroscopic method for analysis of Sitagliptine was adopted in present work. An accurately weighed quantity of Sitagliptine (100mg) was dissolved in 100 mL of 0.1N HCl to generate a stock solution having concentration of 1000 µg /mL. Stock solution (10 mL) was further diluted to 100 mL to produce standard solution having concentration of 100µg/mL. The standard solution was serially diluted with 0.1N HCl to get working standard solutions having concentration of 2, 4, 6, 8, 10 µg/mL. The absorbance of different concentration was analyzed ,it was found that the maximum absorbance is coming at 267.0 nm so it was concluded that 267nm is the λmax for sitagliptine

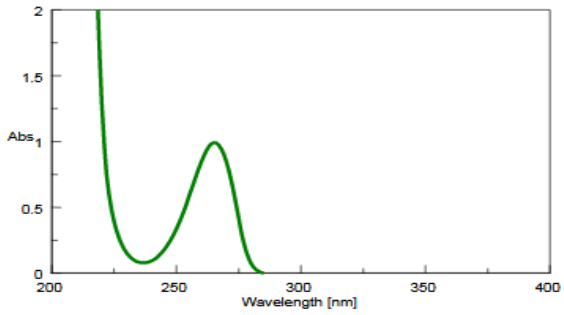


Fig:2. Spectra of Sitagliptine

Construction of Standard curve of Sitagliptine in 0.1 N HCl

An accurately weighed quantity of Sitagliptine (100mg) was dissolved in 100 mL of 0.1N HCl to generate a stock solution having concentration of 1000 µg /mL. Stock solution (10 mL) was further diluted to 100 mL to produce standard solution having concentration of 100µg/mL. The standard solution was serially diluted with 0.1N HCl to get working standard solutions having concentration of 2, 4, 6, 8, 10 µg/mL. The absorbance of the solutions was measured at 267.0 nm using double beam UV visible spectrophotometer against 0.1N HCl as a blank. The plot of absorbance v/s concentration (µg/mL) was plotted and data was subjected to linear regression analysis in Microsoft excel

FTIR study

There is always possibility of drug excipient interaction in any formulation due to their intimate contact. The presence of any drug-polymer interaction was studied by FT-IR spectroscopy. IR spectra for drug and the drug-polymer mixture were recorded in a Fourier Transform Infrared (FT-IR) spectrophotometer (Alpha, Bruckerpvt ltd, Japan) with KBr pellets. The scanning range was 400– 4000 cm^{-1}.

DSC study

The physicochemical compatibilities of the drug and the used excipients were tested by differential scanning calorimetric (DSC) analysis. DSC analysis of the pure drug, polymers and the drug-polymer mixture were performed by using an automatic thermalanalyzer system (Shimadzu DSC-60) to evaluate the drug-polymer interactions. The analysis was performed at a rate of 10 °C per min from 40 °C to 300 °C under a nitrogen flow of 20 ml/min.

XRD study: The XRD pattern for pure sitagliptine,PVP K30 , SLS and optimized formulation were obtained using X-ray diffractometer, The measuring condition were as follows CuKα radiation,nickel filtered, graphaite monochromator 45kV voltage and 40mA current with X celerator detector.All samples are run at $1^0(2\theta)$ min^{-1} from 3^0 to 45^0 (2θ)

Formulation of Controlled Release Osmotic Tablet of Sitagliptine: Materials: Sitagliptine was obtained from Dr.Reddy Lab Hyderabad ,PVP K30 were obtained from Watson Pharmaceuticals, Goa, India, as a gift sample. Sodium chloride, lactose, sodium lauryl sulfate, magnesium stearate, cellulose acetate, sorbitol and Talc was procured from S.D. Fine Chemicals, Mumbai, India. Acetone, ethanol, methylene chloride were purchased from Unichem Biological sciences, Kolhapur. All chemicals and solvents used are of analytical grade.

Method:

Design of Experiment: Two factors, three levels (3^2) full factorial design was used in this optimization technique, the desirability approach was used to generate the optimum settings for the formulation. From the trial batches, three independent variables were found to affect drug release significantly. Concentration of osmotic agent (NaCl) and pore forming agent (SLS) were taken as independent variables. The drug release at 2 hr, 6 hr, and 12 hr are the dependent variables The selected two factors as well as their levels and analyzed response are shown in Table 2and the matrix of the factorial design is represented in Table 3. Each row in the matrix identifies an experiment and each experiment provides a result (response). This design provided an empirical second order polynomial model.

Table:2 Variables in 3^2 full factorial design

Independent Variable			
	Low(-1)	**Middle(0)**	**High(+1)**
X_1 : NaCl (mg)	20	25	30
X_2 : SLS (mg)	10	20	30
Dependent Variable Response			
Y_1 :DR% After 2 hour			
Y_2 : DR% After 6 hour			
Y_3 : DR% After 12 hour			

Table: 3. 3^2 Factorial Design for Sitagliptine Osmotic tablet

	Coded Formulation	
Experiment Run	**X_1**	**X_2**
1	**+1**	**0**
2	**0**	**+1**
3	**0**	**+1**
4	**0**	**-1**
5	**-1**	**-1**
6	**+1**	**-1**
7	**0**	**0**
8	**0**	**0**
9	**-1**	**0**

Preparation of core tablets

Core tablets of Sitagliptine were prepared by wet granulation method. All the ingredients were sieved through # 40 sieve. Individual ingredients, sufficient for a batch of 25 tablets, were weighed on a digital weighing balance. All the ingredients (except PVP K30, magnesium stearate, and talc) were mixed in mortar and pestle using geometric dilution method. The dry blend was granulated with sufficient quantity of PVP K30 which was dissolved in isopropyl alcohol. The powder mass was dried at 60°C in hot air oven for 6 h and passed through # 20 sieve. Then dried granules were mixed with magnesium stearate and talc for 3min. Tablets were prepared by 9mm concave die punch set using rotary tablet punching machine, Tablet weight are adjusted to 200mg.

Table:4 Formulation table for Oral Osmotic Tablet of Sitagliptine

Ingredient (mg)	**FORMULATION**								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Sitagliptine	100	100	100	100	100	100	100	100	100
NaCl	20	25	30	20	25	30	20	25	30
SLS	10	10	10	20	20	20	30	30	30
PVP K30	10	10	10	10	10	10	10	10	10
Starch	50	45	40	45	40	35	35	30	25
Mg. stearate	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5
Total (mg)	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**

Method of Preparation of Tablet Coat Solution

Cellulose acetate and PEG 400 were added to 3/4th of the total volume of acetone and stirred at 35 rpm using propeller stirrer for half an hour till the solution was clear. Magnesium stearate and colouring agent were triturated thoroughly in a mortar and added to the above solution and stirring continued further. Finally, the volume was made up with acetone.

Table:5 Composition of Coating Solvent

Ingridients	Composition
Cellulose Acetate	2% w/v
PEG 400	2% w/v
TiO_2	0.2% w/v
Colouring Agent	0.2%w/v
Acetone	Up to 100ml

Coating of the Core Tablets

Tablet coating was done using coating pan apparatus. Speed of coating pan was set at 30 rpm, and inlet air temperature and flow rate were 50°C and 3.2kg/min, respectively. Spraying rate for coating solution was kept at 4-5 mL/min. Number of tablets per batch was fixed at 50 tablets. Ten tablets of test batch were mixed with 40 dummy tablets. Empty coating pan was run at above set parameters for 5 min. Tablets were loaded to the pan and allowed to gain equilibrium. Coating solution was sprayed at 5mL/min rate for 2-3 seconds. Coating solution on the tablets was allowed to dry for 5min and again sprayed. Approximately 100mL coating solution was used for a batch of 50 tablet.

Characterization of Osmotic Tablet

Hardness: The fracture strength, which is defined as the force, was required to break a tablet by radial compression and was measured with a Monsanto tablet hardness tester in present study. Themean hardness is calculated and expressed as kg/cm^2.

Friability: The friability of the tablets was measured in a Roche friabilator. Tablets of a known weight (w_0) or a sample of 10 tablets are dedusted in a drum for a fixed time (100 revolutions) and weighed (w) again. Percentage friability was calculated from the loss in weight as given in equation as below.

$$F\ \% = \frac{W(i) - W(f)}{W(i)} \times 100$$

W_i =Initial weight W_f =Final Weight

Weight Variation Test: To study weight variation, 20 tablets of each formulation were weighed using an electronic balance individually, calculating the average weight, and comparing the individual tablet weights to the average. The tablets meet the IP test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

Thickness: The thickness of the tablets was determined using a Vernier caliper. 20 tablets were used and mean was calculated. Tablet thickness should not deviate by ±5%.

Determination of Drug Content*:* Ten tablets were accurately weighed and powdered. A quantity of the powder equivalent to 100mg of sitagliptine sodium was weighed accurately and extracted in 100mL water by shaking for 20min. After filtration through Whatman filter paper number 1 and sufficient dilution with water, samples were analyzed spectro-photometrically at 267 nm. Amount of drug present was determined from the calibration curve of sitagliptine

In Vitro Drug Release Study*:*

The release rate of sitagliptine from developed tablets was determined using USP dissolution testing apparatus I (Basket type). The dissolution test was performed using 900mL 0.1M HCl (pH 1.2) for 2 hr and then in pH 6.8 phosphate buffer for 10 hr, at 37 ± 0.5 °C and 100 rpm. A sample (1 mL) of the solution was withdrawn from the dissolution apparatus hourly for 12 h, and the samples were replaced with fresh dissolution medium. The samples were passed through Whatman filter paper after dilution and the absorption of these solutions was measured at 267 nm. The cumulative percentage drug release was calculated.

Curve Fitting Analysis

For the determination of the drug release kinetics from the porous osmotic pump tablet, the in vitro release data were analyzed by zero-

order, first-order, Higuchi, and Korsmeyer and Peppas equations[6].

Zero-Order Release Kinetics

To study the zero-order release kinetics the release data was fitted into the following equation:

$$dQ/dt = K_0, \quad (2)$$

where "Q" is the amount of drug release, "K_0" is the zero order release rate constant, and "t" is the release time. The graph is plotted percentage cumulative drug release (% CDR) versus time.

First-Order Release Kinetics

To study the first-order release kinetics the release rate data are fitted into the following equation:

$$dQ/dt = K_1 Q, \quad (3)$$

where "Q" is the fraction of drug release, "K_1" is the first order release rate constant, and "t" is the release time.

Higuchi Release Model

To study the Higuchi release model the release rate data are fitted into the following equation:

$$Q = K_H t^{1/2}, \quad (4)$$

where "Q" is the fraction of drug release, "K_H" is the release rate constant, and "t" is the release time. The graph is plotted as % CDR versus square root of time.

Korsmeyer and Peppas Kinetics

To study the Korsmeyer and Peppas release kinetics the release rate data are fitted into the following equation:

$$M_t/M_\infty = K_{KP} t^n, \quad (5)$$

where M_t/M_∞ is the fraction of drug release, "K_{KP}" is the release rate constant, "t" is the release time, and "n" is the diffusion exponent related to mechanism of drug release. The graph is plotted as log% CDR versus log time [6].

RESULTS AND DISCUSSION:

Preparation of standard calibration curve of Sitagliptine in 0.1N HCl at 267nm

Calibration curve of Sitagliptine was developed in 0.1 N HCl at 267 nm wave length. Sitagliptine in 0.1 N HCl showed good linearity (r^2=0.992) and intercept 0.002 over the concentration range of 2-12 µg/ml at λmax 267nm. The data for calibration curve are shown in Table- 1 and the calibration curve is shown in Figure-3

Table:1 Standard Curve of Sitagliptine in 0.1N HCI at 267nm

Sr. No	Conc (µg/ml)	Absorbance (Abs)			Average Abs
		1	2	3	
1	2	0.0043	0.0048	0.0041	0.004
2	4	0.0063	0.0068	0.0065	0.006
3	6	0.0086	0.0093	0.0089	0.008
4	8	0.0104	0.0113	0.0111	0.01
5	10	0.013	0.0135	0.0131	0.0132

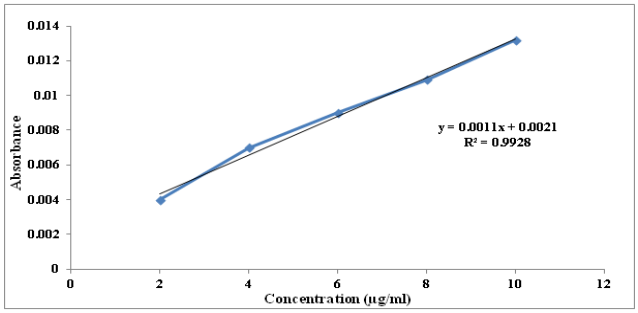


Figure:3 Standard Curve of Sitagliptine in 0.1N HCl at 267nm

Drug -Excipent compatibility study

Drug Polymer Compatibility Studies using DSC

DSC thermograms of pure drug (Sitagliptine) and physical mixtures of drug and excipients (NaCl, SLS, and CA) were studied for their interactions. It was observed that there was no significant drug polymer interaction observed among drug, NaCl, SLS, and CA even at higher temperature. From DSC study, we can see that there is no change in drug's melting peak (169.28 °C–172.77 °C) after the preparation of mixture. There is the no interaction between drug and excipient shown in this study. So, we can conclude that drug is compatible with all polymers. DSC-excipients interactions play a vital role in the release of drug from formulation.

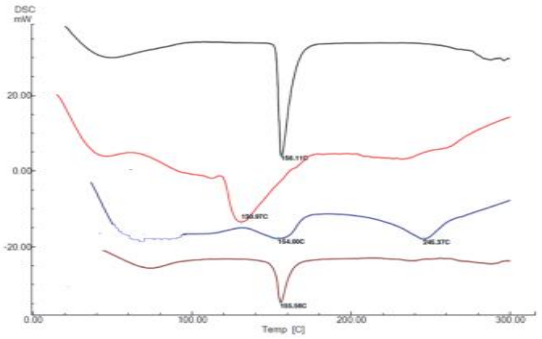


Fig. No. 4 DSC Profile

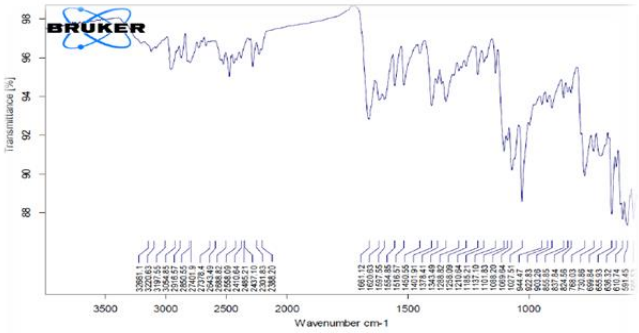


Fig. No 6 FTIR Of optimized formula

Drug Polymer Compatibility Studies using FTIR

Fourier transform infrared spectroscopy has been used to study the physical and chemical interactions between drug and the excipients used. The pure Sitagliptine and its mixture with excipients mixed separately with IR grade of KBr and were scanned over a range of 400-4500 cm-1 using FTIR instrument (Alpha, Brucker Pvt ltd, Japan). The drug exhibits peaks due to amide group, alcohol group and C-H, Ar-O-CH, C=C and C-O-C stretching. It was observed that there were no or very minor changes in drug main peaks in the IR spectra of a mixture of drug and pure drug The FTIR study revealed no physical or chemical interactions of Sitagliptine with excipient each as evident from Figure :5 &6

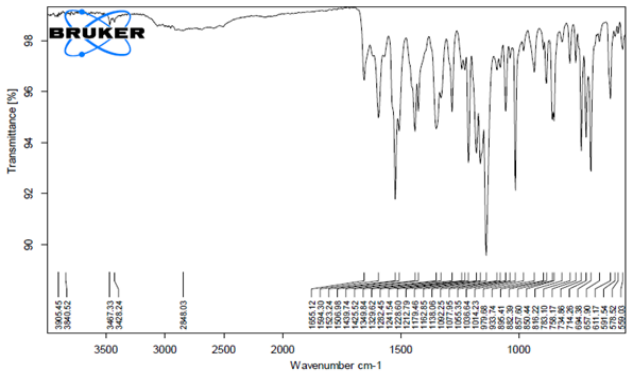


Fig. No 5 FTIR Of Sitagliptine

XRD Results

The pure sitagliptne showed numerous characteristics high intensity diffraction peaks demonstrating crystalline nature of the drug in figure :7,The diffused peaks of optimized formulation indicate amorphization of drug which leads to higher solubility

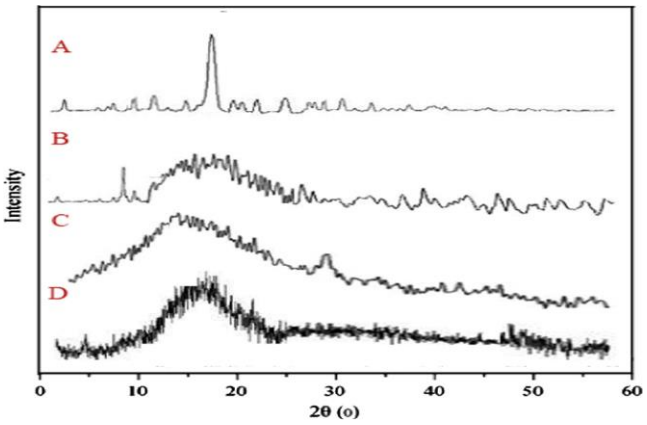


Fig. No 7 a) Sitagliptine
b) **PVPK30**
c) **SLS**
d) **Optimized Formulation**

Pre formulation Study results

In this research, all nine formulation were subjected for various pre-compressional evaluations such as angle of repose, bulk and tapped density, compressibility index and Hausner's ratio. The findings of pre-compression evaluation was given in **Table-6,** Angle of repose was found to be ranging from 29.02° to 36.34° all formulation shows good flow property. Carr's index was found to be ranging from 10.07% to 19.62 % for the powders of all the formulations.

Post compression results: The results of physical evaluation of tablets is given below in **Table-7** The tablets of different batches were found uniform with respect to hardness within the range of 4.93 to 5.83 kg/cm^2. Another measure of a tablet's strength is friability. Results of friability test were also has been found within limit. In weight variation test, the pharmacopoeial limit for percentage deviation for tablets of more than 200 mg is ±5% and all the formulations were found to comply with the specifications given in I.P. for weight variation test. Good uniformity in drug content was found among the formulations, and percentage of drug content was more than 95%. All the tablet formulations showed acceptable pharmaco-technical properties

Effect of Formulation Variable on Drug Release at 2hr (Y1): The relationship between formulation variables ($X1$ and $X2$) and $Y1$ was further elucidated using 3D surface plot. From Figure 11&12 it can be concluded that factor NaCl ($X1$) had more osmotic effect on drug release while SLS ($X2$) had significant effect on drug release.

Effect of Formulation Variable on Drug Release at 6 hr (Y2): The relationship between formulation variables ($X1$ and $X2$) and $Y2$ was further elucidated using 3D surface plot. From Figure13&14 it can be concluded that factor SLS($X2$) had more pore forming effect on drug release while NaCI ($X1$) had little effect on drug release.

Effect of Formulation Variable on Drug Release at 12 hr (Y3): It can be concluded that factor NaCl ($X1$) has more effect on drug release than SLS ($X2$).

Effect of pH on Drug Release: When formulation F9 as subjected to in vitro release studies in buffers with different pH and distilled water, no significant differences in the release profiles were seen compared to that in phosphate buffer pH 6.8.Thus the fluid in different parts of the GI tract will scarcely affect drug release from the osmotic system.

Table:6 Micromeritic Results of different batches of Sitagliptine Osmotic Tablet

Batch	Angle of Repose	Bulk density(gm/cm^3)	Tapped density(gm/cm^3)	Carr;s Index	Porosity(%)
F1	31.03±0.03	0.187±0.13	0.289±0.13	11.12±0.13	11.43
F2	17.43±0.03	0.187±0.03	0.299±0.33	10.02±0.03	13.45
F3	28.13±0.03	0.197±0.03	0.219±0.03	12.12±0.23	12.46
F4	29.13±0.13	0.129±0.03	0.289±0.03	13.12±0.33	10.13
F5	28.33±0.03	0.187±0.03	0.291±0.04	13.12±0.43	11.43
F6	27.33±0.03	0.183±0.02	0.279±0.13	11.12±0.13	11.43
F7	28.33±0.03	0.189±0.03	0.283±0.23	11.12±0.13	11.43
F8	28.33±0.03	0.167±0.03	0.299±0.13	11.12±0.13	11.43
F9	28.33±0.03	0.186±0.03	0.279±0.03	11.12±0.13	10.43

Table:7 Evaluation of Core osmotic tablet of Sitagliptine

Batch	Hardness (kg/cm^2)	Friability (%)	Thickness (mm)	Drug Content (%)	Weight (mg)
F1	8.13	0.31	3.91	91.33	200
F2	8.27	0.85	3.92	93.44	201
F3	9.11	0.71	3.90	92.67	200
F4	8.01	0.43	3.93	94.32	202
F5	8.22	0.75	3.90	98.33	201

F6	7.99	0.76	3.92	98.33	203
F7	8.32	0.86	3.92	98.33	202
F8	9.01	0.87	3.90	98.33	201
F9	9.11	0.33	3.91	98.33	200

Table:8 In-vitro Release Profile of Different Formulation Sitaglptine Osmotic Tablet

Time (hr)	**% of Drug Release**								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
1	20	10	22	12	20	22	20	18	24
2	22	28	31	21	32	32	28	21	36
3	42	32	36	46	56	47	42	38	56
4	45	57	42	52	72	49	57	41	62
6	68	70	51	59	89	69	70	50	78
8	74	86	62	68	98	77	86	68	81
10	86	98	70	74	-	86	99	70	98
12	90	-	82	86	-	90	-	79	100
14	92	-	85	90	-	93	-	86	-

Table: 9 Release Profile of Different Formulation Sitaglptine Osmotic Tablet Kinetic Modelling of Optimized Formulation F9

Parameter	**Zero-order**	**First-order**	**Higuchi**	**Korsmeyer-Peppas**
Sum of residuals	1314.416	346.8983	205.599	75.4920
Correlation coefficient (r)	0.9781	0.9821	0.9905	0.9960
***R* square ($r2$)**	0.940	0.785	0.785	0.838
F	109.534	28.901	17.132	6.89

Table 10: Results of Stability Study

Parameter	**Initially**	**After 30 days**
Weight variation (n = 10)	200	198
Diameter (mm)	10	10
Thickness (mm)	5	4.9
Hardness (kg/cm2)	6.8	6.7
$Y3$ (% drug release at 12 hr)	98.72	95.72

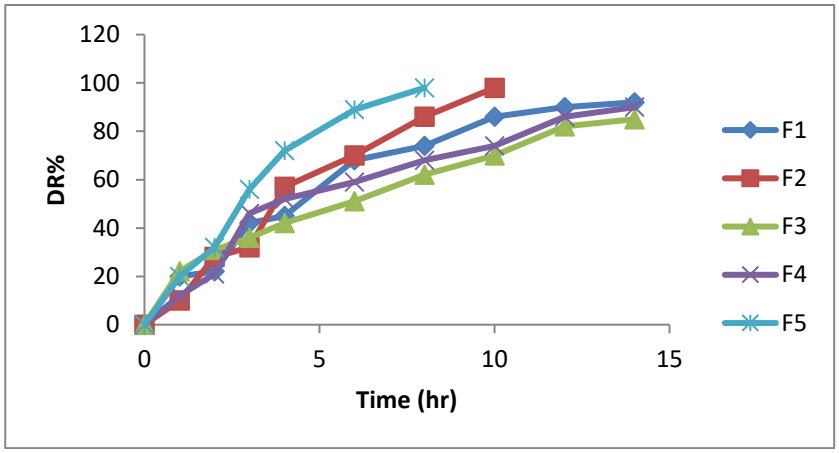


Fig. No.8 In-vitro drug release profile of (F1-F5)

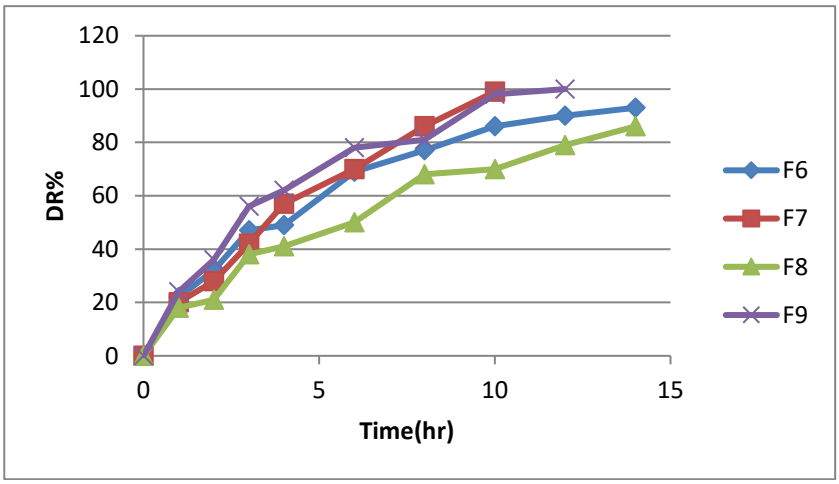
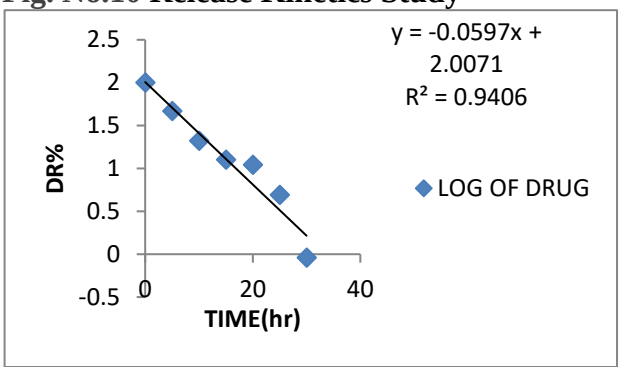
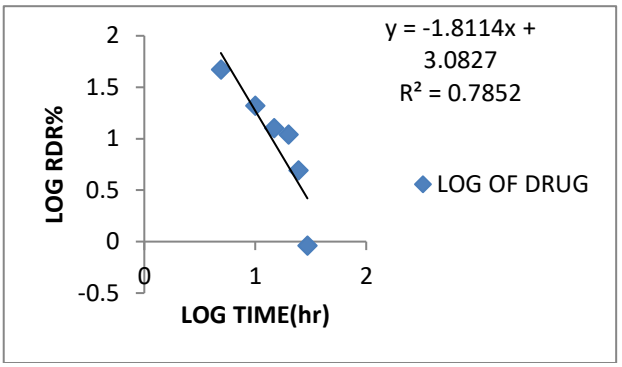
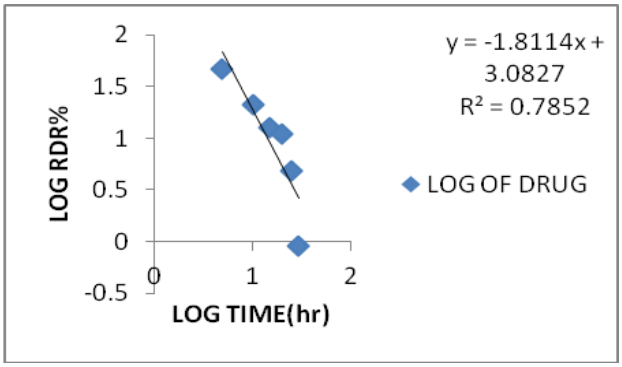


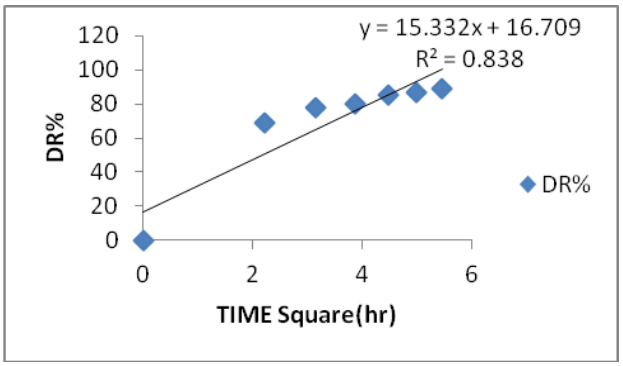
Fig. No.9 In-vitro drug release profile of (F6-F9)

Fig. No.10 Release Kinetics Study









Optimization

ANOVA for Quadratic model for DR% 2hr **Response 1: DR% 2hr**

Source	Sum of Squares	df	Mean Square	F-value	p-value	Significant
Model	59.44	5	11.89	0.1988	0.0430	**Significant**
X_1-NaCl	20.17	1	20.17	0.3372	0.0122	
X_2-SLS	10.67	1	10.67	0.1783	0.0713	
X_1X_2	25.00	1	25.00	0.4180	0.0640	
X_1^2	0.0556	1	0.0556	0.0009	0.0776	
X_2^2	3.56	1	3.56	0.0594	0.0231	
Residual	179.44	3	59.81			
Cor Total	238.89	8				

Fig. No.11 Counter Plot for DR% 2hr

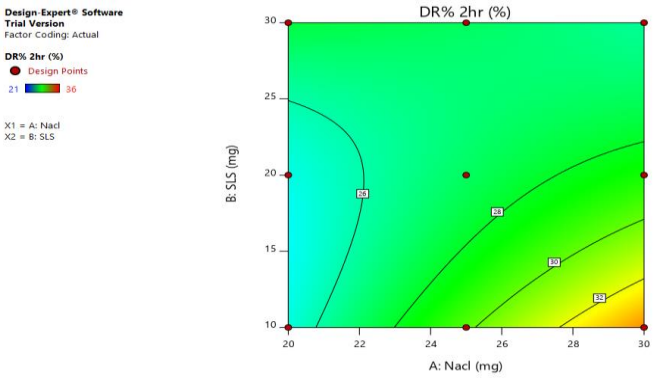
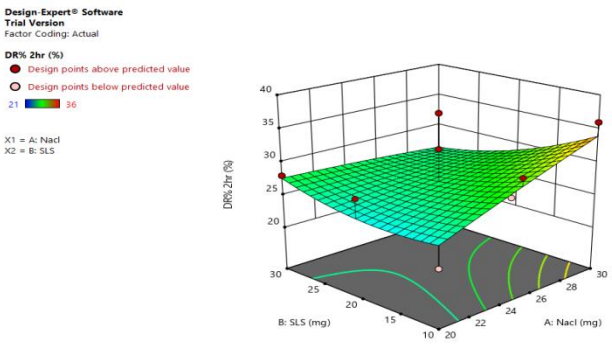


Fig. No.12 3D PLOT for DR% 2hr

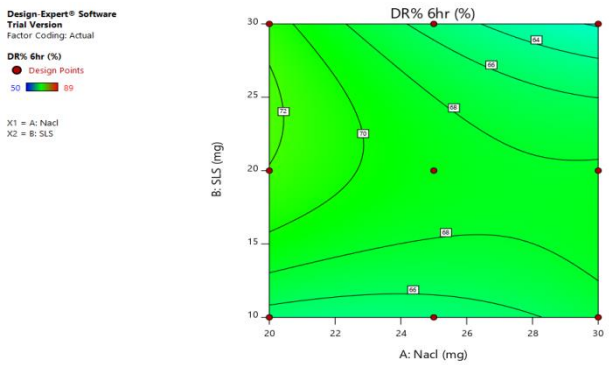


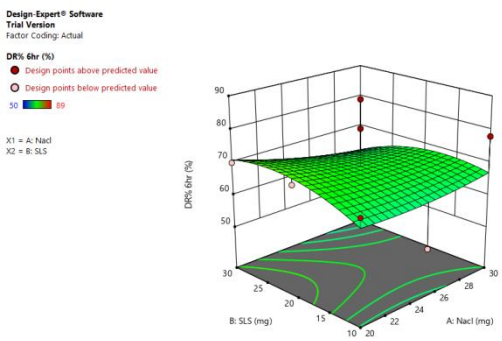
ANOVA for Quadratic model for DR% 6hr **Response 2: DR% 6hr**

Source	Sum of Squares	df	Mean Square	F-value	p-value	Significant
Model	82.69	5	16.54	0.0430	0.0477	**Significant**
X_1-NaCl	20.17	1	20.17	0.0524	0.0336	
X_2-SLS	0.1667	1	0.1667	0.0004	0.0847	
X_1X_2	30.25	1	30.25	0.0786	0.0974	
X_1^2	2.72	1	2.72	0.0071	0.0383	
X_2^2	29.39	1	29.39	0.0764	0.0102	
Residual	1154.19	3	384.73			
Cor Total	1236.89	8				

Fig. No.13 Counter Plot for DR% 6hr

Fig. No.14 3D PLOT for DR% 6hr

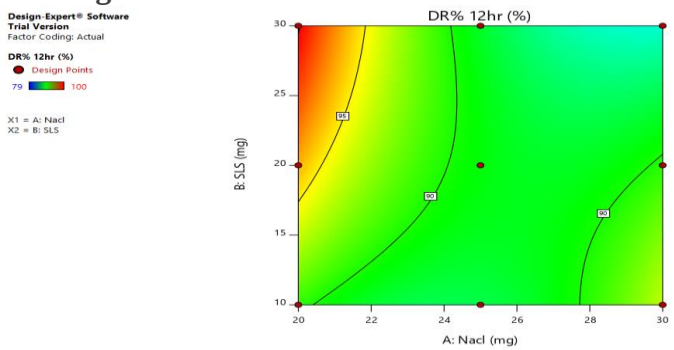


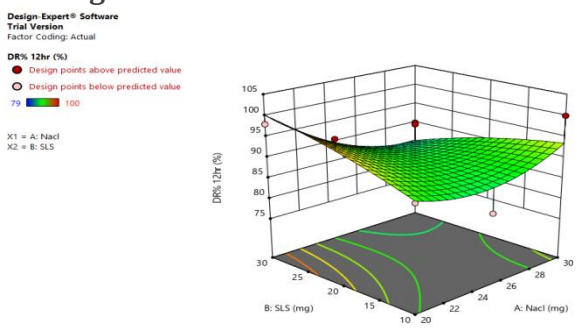


ANOVA for Quadratic model for DR% 12hr **Response 3: DR% 12hr**

Source	Sum of Squares	df	Mean Square	F-value	p-value	Significant
Model	169.67	5	33.93	0.3139	0.0578	**Significant**
X_1-NaCl	54.00	1	54.00	0.4995	0.0307	
X_2-SLS	0.6667	1	0.6667	0.0062	0.0424	
X_1X_2	81.00	1	81.00	0.7492	0.0504	
X_1^2	32.00	1	32.00	0.2960	0.0242	
X_2^2	2.00	1	2.00	0.0185	0.0404	
Residual	324.33	3	108.11			
Cor Total	494.00	8				

Fig. No.15 Counter Plot for DR% 12hr **Fig. No.16 3D PLOT for DR% 12hr**





Effect of Agitation Intensity on Drug Release

The release profile of sitagliptine from the optimized formulation F9 was independent of the agitational intensity of the release media.

Stability Study

After the 1-month storage of formulation F22, values of all parameters like hardness, diameter, thickness, % drug content, and friability were checked periodically and found to be almost similar to the initial values. The drug profile was similar to the initial profile There was not any significant change in any value and also no changes in the physical appearance. So it can be said that formulation is stable

CONCLUSION: The observed independent variables were found to be very close to predicted values of optimized formulation which demonstrates the feasibility of the optimization procedure in successful development of porous osmotic pump tablets containing Sitagliptine as model drug by using sodium chloride (30mg) as osmotic agent, sodium lauryl sulphate (30mg) as pore former, cellulose acetate (2%) as coating agent, and control membrane permeability. Batch F9 was selected as optimized batch. Stability studies also revealed that optimized formulation is stable. , so it concludes that porous osmotic pump tablets of antidiabetic drugs were successfully developed.

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