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Development and optimization of Osmotically controlled self-pore forming tablet of Vildaglitpin

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Abstract:
Vildagliptin is an oral antihyperglycemic agent which is incorporated in the osmotic controlled release drug delivery system. Drug passes all the parameters of preformulation studies. Vildagliptin is compatible with other excipients analysed by various studies like FTIR analysis.
Core tablet is prepared by wet granulation technique with composite formula by 3/2 factorial design. Core tablet is coated with spray technique using described coating solution.
According to post compression parameters like dissolution test, SEM and stability study F7 is optimized formulation which shows 97.32 % drug release after 12 hrs.
Keywords: Vildaglitpin, Osmotically controlled, self-pore, optimization.

INTRODUCTION

Osmotic drug delivery system (ODDS) is one of the most advanced drug delivery systems that utilize osmotic pressure as a driving force for controlled delivery of drugs. [1]
Controlled Porosity osmotic pump (CPOP) tablets is an osmotic tablet wherein the delivery orifices are formed in situ through leaching of water soluble pore forming agents incorporated in semi permeable membrane [2]. Main advantages of CPOP are reduced stomach irritation, no complicated laser- drilling. CPOP consists of osmotic core with drug surrounded by a semi permeable membrane drilled with a delivery orifice. Controlled porosity is accomplished by the use of different channeling agent in the coating [3]. Controlled Porosity osmotic pump (CPOP) tablets Follows zero order kinetics after an initial lag.The delivery of drug may be delayed or pulsatile [4].
Vildagliptin is oral anti-hyperglycemic agent (anti-diabetic drug) of the new dipeptidyl peptidase-4 (DPP-4) inhibitor class.It is rapidly absorbed following oral administration with an oral bioavailability of greater than 90%.Vildagliptin has a short half-life of 90 min only [5].Long-term therapy in hyperglycemia by Vildagliptin may result in poor patient compliance since it has low bioavailability and short half-life, leading to increased frequency ofadministration.Controlled release Vildagliptin formulation is therefore necessary for improving patient compliance and reducing frequency ofadministration.Hence, the present study was intended towards the development of controlled release self pore forming tablet of vildagliptin.

MATERIALS AND METHODS

Vildagliptin was gifted by Aurobindo Pharma., Hyderbad, while all other chemicals were purchased from the market.

Methods

PreformulationStudy
Preformulation studies: Drug Identification and Characterization [6, 7, 8, 9]
Fourier Transform Infra-Red (FTIR) analysis

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The FTIR study of pure drug sample was carried out using FTIR Spectrophotometer. The pure drug was mixed with IR grade KBr. This mixture was then scanned over a wave number rangeof4000 to 400 cm^{-1}. The FTIR spectra of drug was compared with standard FTIR spectra.

Differential Scanning Calorimetry (DSC)

DSC scans were recorded by using Differential scanning calorimeter. Samples weighing 5 mg were sealed in aluminium pans and heated to 550°C at rate 10°C/min. The equipment was calibrated using indium. Samples were heated from 50 to 550°C. If required, it was cooled to -10°C and then heating was continued to 550°C.

Analytical Method for Estimation of theDrug:

Standard Calibration Curve:

Vildagliptin (10 mg) was dissolved in 0.1N HCl and volume was made up to 100 ml. From above solution various dilutions were prepared to get concentrations of 5, 10, 15, 20 and 30 mcg/ml. The absorbance of the various solutions was measured against 0.1N HCL as a blank at 217 nm using double beam UV visible spectrophotometer. The graph of absorbance v/s concentration was plotted and data were subjected to linear regression analysis.

Drug: Excipient Compatibility Study

FTIR analysis

The drug and drug-polymer mixture (1:1) were mixed with dried potassium bromide and compressed under 10-ton pressure for 5 min in a hydraulic press to form a transparent pellet. These pellets were scanned in the region of 4000 to 400 cm-^{1}using a FTIR Spectrophotometer.

Formulation Development and Optimization

After preliminary studies the formulations were designed according to the 3^2 full factorial design, allowing a simultaneous evaluation of the two formulation variables and their interaction. The experimental design with the corresponding formulation is outlined in Table. The effect of the independent variables, viz., Sodium chloride (X_1) and HPMC E5 LV (X_2) on the dependent variable, *in vitro* floating time and drug release (y_1) was evaluated.

A core tablet of Vildagliptin was prepared by wet granulation method as per the following steps

1) Vildagliptin was weighed accurately and passed through # 40 mesh.
2) Accurately weighed lactose, HPMC EV5 and sodium chloride was passed through # 40 mesh and mixed with Vildagliptin in cage blender for 10 min at 20 rpm.
3) Accurately weighed PVP K-30 was dissolved in IPA to prepare binder solution.
4) The above blend was granulated using prepared binder solution.
5) The granules were dried in the tray drier at 65ºC, till LOD of the granules lies between 2% w/w to 3% w/w.
6) Dried granules were passed through # 20 mesh using Oscillating Granulator.
7) Accurately weighed magnesium stearate and talc was pass through # 60 mesh. Above blend was lubricated in cage blender for 3 min at20 rpm with magnesium stearate and talc.
8) The granules were evaluated for pre compression parameters and compressed.

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9) Compression was done on 8 station D- Tooling machine using 12/32" FFBE (Flat Face Beveled Edge) punch set. Weight of the tablet was kept to 275 mg.

Table1 : Composition of Controlled porosity osmotic pump tablet as per 3^2 Full Factorial Design (All values are expressed in mg)

Ingredients	Formulation code								
Quantity(mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Vildagliptin	50	50	50	50	50	50	50	50	50
Sodium Chloride	10	10	10	20	20	20	30	30	30
HPMC EV5	50	75	100	50	75	100	50	75	100
PVP 30	10	10	10	10	10	10	10	10	10
Pharmatose 200	150	125	100	140	115	90	130	105	80
Magnesium Stearate	2	2	2	2	2	2	2	2	2
Talc	3	3	3	3	3	3	3	3	3
Total Weight (mg)	275	275	275	275	275	275	275	275	275

Tablet Compression

Compression cycle was performed and machine parameters were optimized as per the IPQC check. Adjustments were done accordingly to finally compress the granules. Tablets were collected in tray and stored in tray dryer at 400C for one day. Then stored at room temperature.

Core Tablet Coating

Preparation of coating solution

The core tablet was coated with coating solution by spray coating technique. Coating solution was prepared by dissolving cellulose acetate in Acetone and stirred properly to dissolve the polymer. To this solution 1% w/v of PEG 400 and sorbitolwas added. Four trial coating solutions were prepared as per composition mentioned in the table.

Table 2: Composition of Coating solution

Ingredients	C1	C2	C3	C4
Cellulose Acetate (% w/v)	2	4	2	4
Polyethylene glycol 400 (% w/v)	1	1	1	1
Sorbitol (% w/v)	0.5	0.5	1	1
Acetone (ml)	100	100	100	100

Optimization of composition of coating of compressed tablets

Formulation F1 was selected prototype formulation for optimization of coating solution. Tablets were coated to check quality of coating to optimize the composition. 50 tablets were taken in laboratory stainless steel pear shaped baffled coating pan. The pan speed was adjusted to 25rpm to set in tumbling bed of tablet. The inlet temperature was kept 45^0C. The coating solution was sprayed manually on the bed with the help of spray gun. Intermittent spraying and drying technique was used for uniform coating. The coating was continued till 4% weight gain was achieved than that of core tablet. The coated tablets wee then stored in hot air oven at 55^0C for further drying for 24 hours.

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Coating of Compressed tablets

Coating of compressed tablets was done using optimized coating composition as per the same procedure mentioned above for nine formulation batches.

Dissolution Test

The USP 24 (8) method for enteric coated tablets (basket method, 75 rpm, 37±0.5°C) was used for all experiments. The study was conducted in 750 mL 0.1 N HCl for 2 hr, followed by dissolution at pH of 6.8 (adjusted by addition of 250 mL of 0.2 M trisodium phosphate). At suitable interval 5 mL aliquot was removed and 5 mL of fresh media was added to maintain original volume. Dissolution was conducted in 0.1M HCl for 2 hrs and while after 2 hr dissolution was conducted in phosphate buffer pH 6.8 and aliquots were analyzed for Vildagliptin at a λ_{max} 217 nmUV spectrophotometrically.

Scanning Electron Microscopic Study

The coated tablets were observed under scanning electron microscope (SEM, Hitachi, Japan). The tablets were observed at 20 kV by sprinkling sample on the aluminum stubs having double adhesive tape and subsequent evaporation of gold palladium alloy in the ion sputter unit. Study was conducted with tablets before and after dissolution study (1 hr) to evaluate formation of pores on the surface.

Stability studies

The optimized formulation was subject to stability evaluation at elevated humidity and temperature conditions as per ICH guidelines. Tablet formulations were kept at 40±2 ^{0}C / 75±5% RH in aluminum foils for the period of 3 months. Samples were analysed periodically for physical appearance, drug content and in vitro drug release profile.

RESULTS ANDDISCUSSION

Drug Identification and Characterization

DSC Study of Vildagliptin

The DSC thermogram of pure drug is shown in the Figure. The curve showed melting of drug between 153-155°C and endothermic peak at 154.21^{0}C. The values are corresponding to the melting point of pure drug and thus confirmed the identity and purity of the drug.

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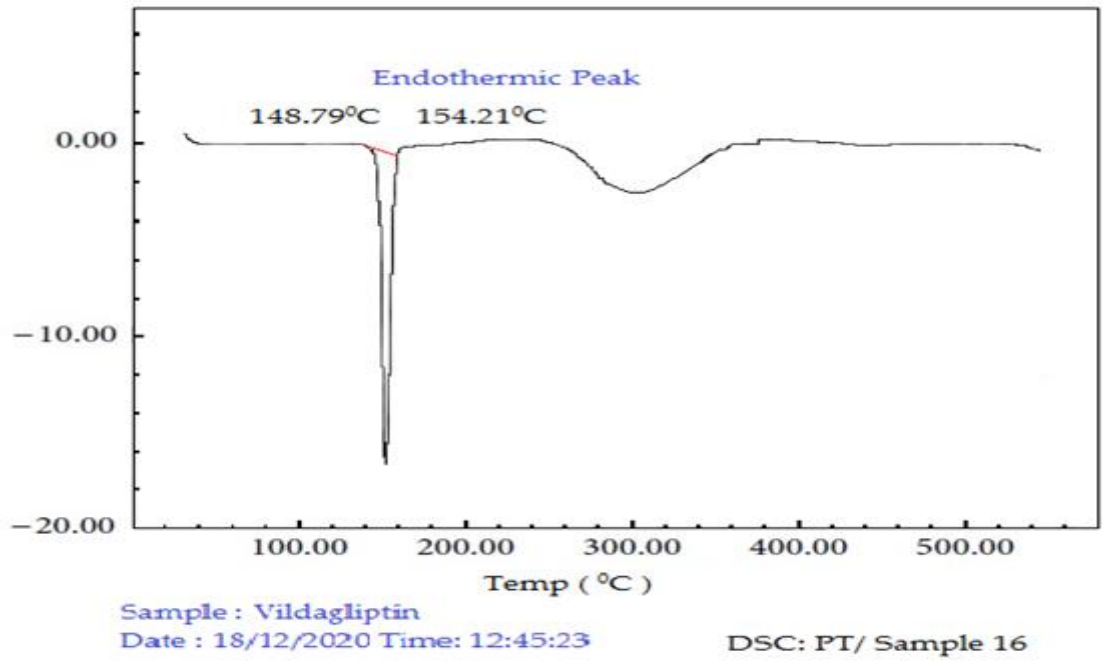

Figure 14: DSC Curve of Pure Vildagliptin

Fourier Transform Infra-Red (FTIR) analysis

FT-IR spectra of pure drug was compared with reference reported values for Vildagliptin. FTIR of pure Vildagliptin showed characteristic sharp peaks at 3345.14 cm^{-1}due to N-H stretching vibrations, 2919.85 cm^{-1} corresponding to C-H stretching, 1681.84 cm^{-1} due to carbonyl group vibrations and 1255.28 cm^{-1} corresponding to C-H (aliphatic) stretching vibrations. The peak observed in the FTIR spectra of pure drug were found to be matching with reference reported values for Vildagliptin, thus confirming identity and purity of drug.

Table 3: Interpretation of FTIR spectra

WAVE NUMBER (cm^{-1})	INTERPRETATION
3345.14	N-H stretching vibrations
2919.85	Methyl Symmetrical Stretching
1681	Aromatic ketone C=O stretching
1255.28	C-H stretching [aliphatic],
851	CH3 symmetrical

UV Spectrophotometric Analysis

Calibration Curve

The calibration curves of Vildagliptin in 0.1N HCL and Phosphate buffer solution pH 6.8 at 217 nm were developed. It was found to obey Beer's law in prepared concentration range 5- 30 µg/ml.

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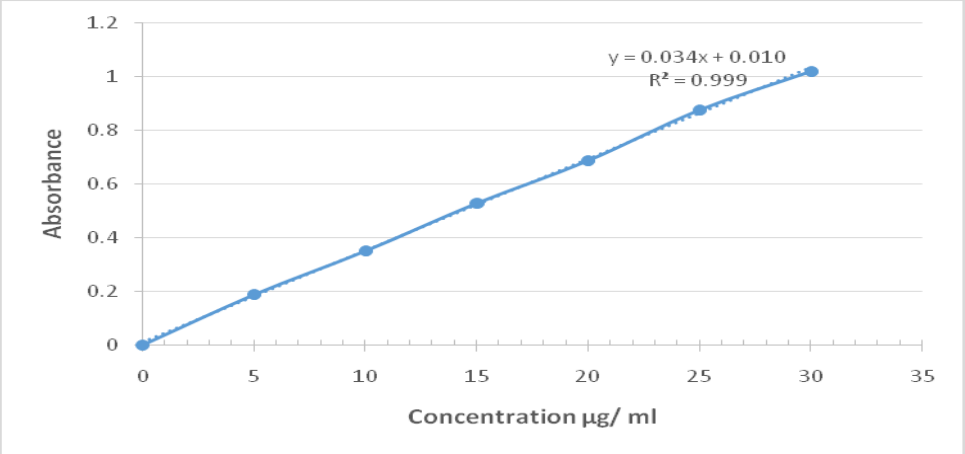

Figure : Standard calibration curve of Vildagliptin in 0.1NHCl

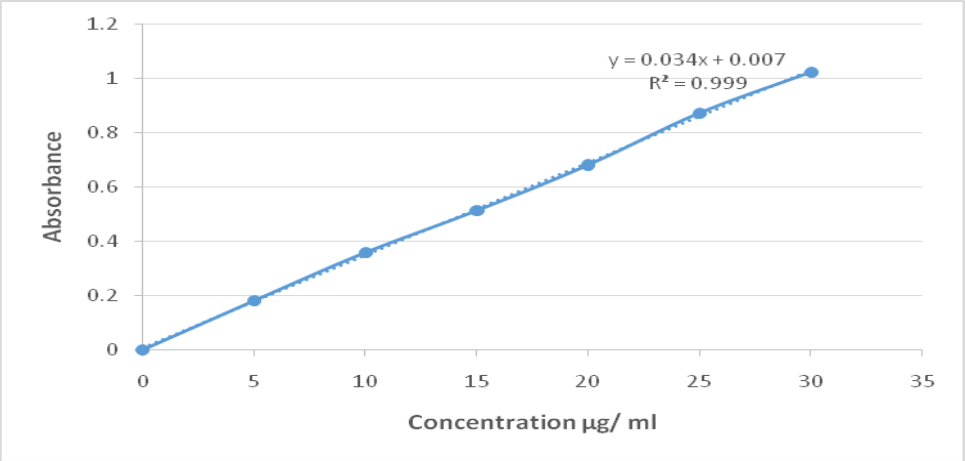

Figure : Calibration Curve of Vildagliptin in 6.8 phosphate buffer

Drug –Excipient Compatibility Study

Physical observation of mixture

Physical mixtures of drug and excipient were observed physically after 1 month. Vildagliptin was found to be compatible with all the excipients used in our formulation and metformin. No change in color or physical appearance was seen.

FTIR Spectrophotometric Study

FTIR of pure Vildagliptin showed characteristic sharp peaks at 3345.14 cm^{-1}due to N-H stretching vibrations, 2919.85 cm^{-1} corresponding to C-H stretching, 1681.84 cm^{-1} due to carbonyl group vibrations and 1255.28 cm^{-1} corresponding to C-H (aliphatic) stretching vibrations. The FTIR spectra of drug with excipients showed that there was no change in the FTIR pattern of all the functional groups of Vildagliptin. The peaks observed in the FTIR spectra of pure drug were found in FTIR spectra of physical mixture of drug and excipients.

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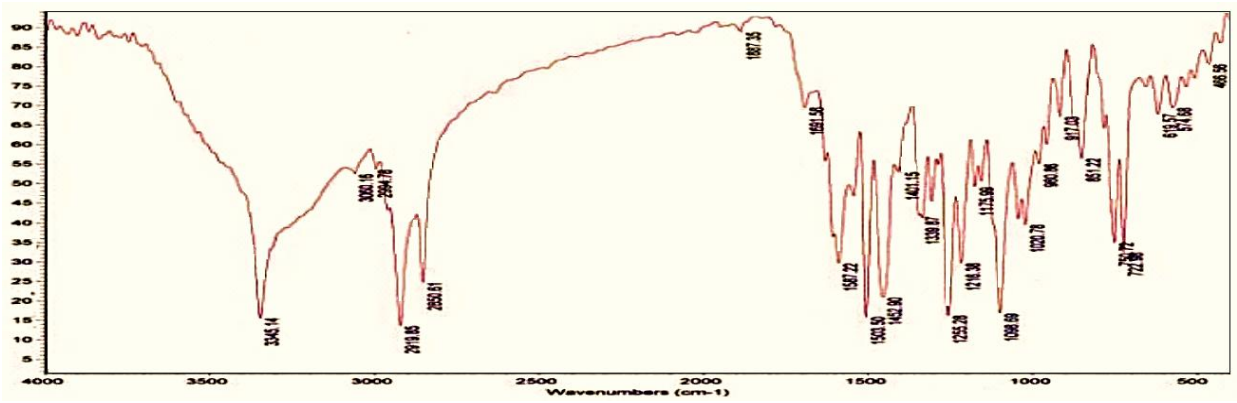
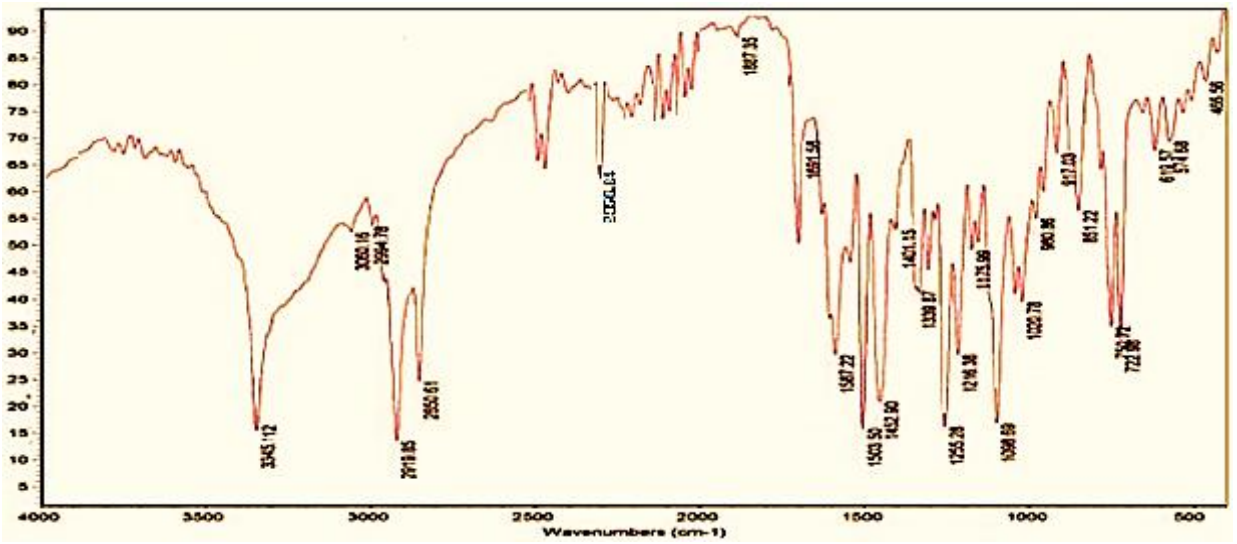
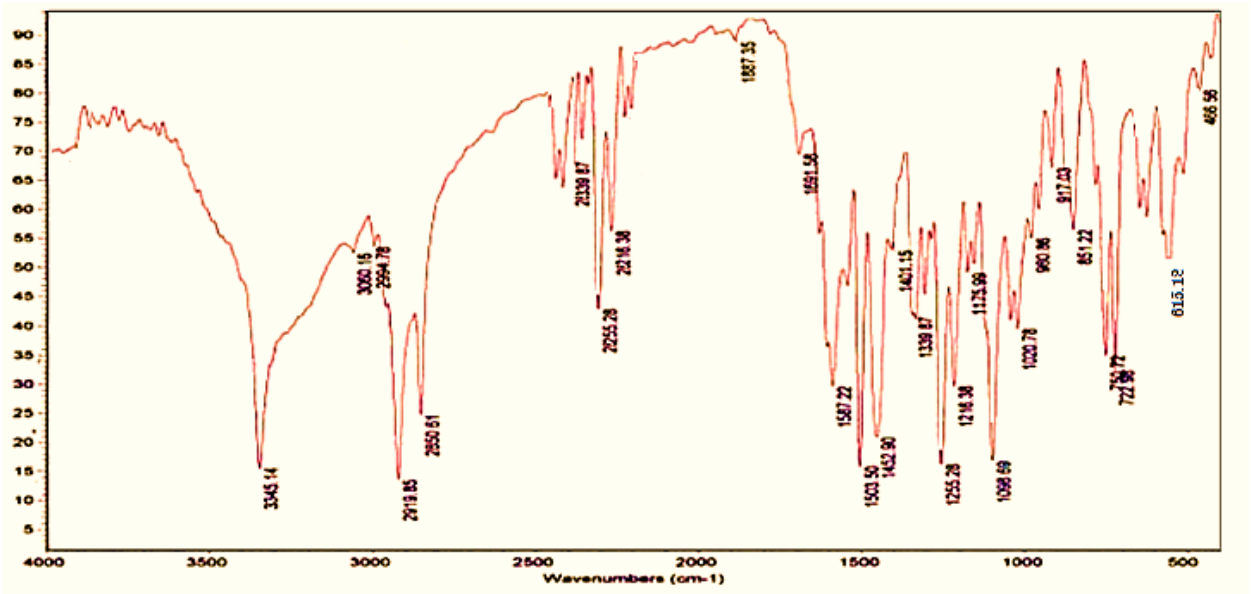


(A)



(B)



(C)

Figure : FTIR spectra of (A) Vildagliptin B) Vildagliptin + Pharmatose 200 C) Vildagliptin + HPMC EV5

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Formulation Development and Optimization

Evaluation of precompression characteristics of granules

The granules prepared for nine batches of tablet formulations were evaluated for flow and compression properties. All batches of granules showed excellent flow properties with angle of repose value between 27-29˚. The packaging capacity of granules was evaluated by measuring bulk and tapped density and found respectively between 0.38- 0.41 gm/ cm^3 and 0.43-0.46 gm/ cm^3. Compressibility of granules was determined using bulk and tapped density. The carr's index was found in the range of 10-11% suggesting excellent compression ability of granules. The Hausner's ratio values were found in the range of 1.12-1.13, indicating excellent flow and compression properties of granules. The results are summarized in the table 4.

Table 4: Evaluation of Granules for Tablets

Formulation code	Angle of repose(θ°) Mean± S.D	Bulk density gm/cm3) Mean± S.D	Tapped density (gm/cm3) `Mean± S.D	Compressibility index (%) Mean± S.D	Hausner's ratio Mean± S.D
F1	28.94±0.64	0.41±0.012	0.46±0.01	10.86957	1.121951
F2	28.77± 0.75	0.39±0.019	0.44±0.011	11.36364	1.128205
F3	29.21±0.85	0.38±0.017	0.44±0.012	11.62791	1.131579
F4	27.91±1.07	0.40±0.019	0.45±0.013	11.11111	1.125
F5	29.44±0.51	0.39±0.011	0.44±0.014	11.36364	1.128205
F6	28.39±0.69	0.38±0.015	0.43±0.012	11.62791	1.131579
F7	28.24±068	0.41±0.02	0.46±0.014	10.86957	1.121951
F8	29.52±0.39	0.40±0.015	0.45±0.016	11.11111	1.125
F9	28.88±0.63	0.39±0.013	0.44±0.011	11.36364	1.128205

Post Compression Evaluation of Uncoated Tablet

Uncoated tablets were evaluated for Weight variation, Hardness, Thickness,friability and Drug content and found within the acceptable limit. Post compression evaluation data is summarized in the table 5.

Table 5: Evaluation of uncoated tablet

Formulation Code	Average Weight (mg) Mean ± S.D	Weight variation %	Hardness ($kg/cm^{2)}$ Mean± S.D	Thickness (mm) Mean± S.D	Friability (%) Mean± S.D	Drug content (%) Mean± S.D
F1	275.11±1.24	0.22	3.66±0.17	3.61±0.02	0.21±0.022	99.43±0.04
F2	275.21±1.64	0.26	3.83±0.19	3.60±0.02	0.14±0.022	99.32±0.05
F3	275.54±1.71	0.30	3.89±0.13	3.61±0.02	0.12±0.04	99.41±0.05
F4	275.47±1.82	0.35	3.79±0.17	3.61±0.04	0.29±0.046	99.40±0.04
F5	275.53±1.30	0.41	3.87±0.16	3.61±0.03	0.16±0.023	98.61±0.03
F6	275.77±1.42	0.48	3.75±0.18	3.61±0.02	0.17±0.04	98.86±0.05
F7	275.24±1.27	0.34	3.84±0.18	3.61±0.01	0.19±0.04	99.11±0.03
F8	275.35±1.19	0.36	3.91±0.1	3.61±0.01	0.18±0.047	99.12±0.04
F9	275.62±1.32	0.37	3.84±0.11	3.60±0.03	0.17±0.063	98.81±0.06

Evaluation of Coated Tablet Formulation

Optimization of Coating composition

Formulation F1 was coated with four coating solutions to check the quality of film, uniformity of coating and film thickness.

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Table : Optimization of coating solution

	C1	C2	C3	C4
Physical Appearance	Thin and Non uniform coating on core tablet	Uniform and smooth coating surface	Thin and non uniform coating	Uniform coating and smooth coating surface
Film thickness	0.31	0.58	0.29	0.59
Weight variation	0.43	0.41	0.44	0.42

Based on the findings of the trial batches prepared with varying concentration of cellulose acetate and sorbitol, composition of C2 batch was optimized for further coating of tablets.

Table 6: Evaluation of Coated tablet

Formulation	Average Weight (mg) Mean± S.D	Weight Variation %	Thickness of coated tablet Mean± S.D	Thickness of film(mm)
F1	286.95±1.35	0.41	4.19±0.01	0.58
F2	286.60±1.09	0.36	4.20±0.01	0.6
F3	285.95±1.21	0.35	4.20±0.02	0.59
F4	286.60±1.15	0.35	4.21±0.01	0.6
F5	285.05±1.17	0.36	4.20±0.01	0.59
F6	286.10±1.47	0.40	4.20±0.02	0.59
F7	286.80±1.08	0.34	4.21±0.01	0.6
F8	287.63±1.03	0.39	4.20±0.02	0.59
F9	258.31±1.12	0.380	4.14±0.012	0.61

***In-Vitro* Drug Release**

In vitro drug release profile is illustrated in tablet. It was observed that as the concentration of osmogen was increase the drug release also increase. Sodium chloride concentration was varied as 10 (F1 to F3), 20 (F4 to F6) and 30 mg (F7 to F9). The cumulative percentage drug release was found to be 80, 77, 75, 94, 89, 87, 97, 91 and 90 respectively for formulation F1 to F9 at the end of 12 hrs.

It was also observed that with increase in concentration of HPMC EV5, the cumulative percentage drug found decreasing, as was seen while comparing the F1, F4, F7 (HPMC EV 5 amount of 50 mg), F2, F5, F8 (HPMC EV 5 amount 75 mg) and F3, F6 and F9 (HPMC EV amount 100mg)

Table 7: *In-vitro* dissolution data (cumulative percent release) (n=3)

Sr N	Time hrs.	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)	F7 (%)	F8 (%)	F9 (%)
Dissolution data in 750 mL of 0.1M HCl										
1	**0.5**	2.1± 0.2	2.1±0.14	1.9±0.54	2.4± 0.4	2.4± 0.33	2.3± 0.09	2.6± 0.12	2.5± 0.09	2.4 ± 0.11
2	**1**	7.7±0.21	7.8±0.58	7.2± 0.35	8.8 ± 0.41	8.5± 0.21	7.8± 0.17	9.1± 0.54	9.6± 0.61	9.3± 0.42
3	**2**	17.05± 1.02	17.02±0.68	17.25± 1.44	21.19± 1.04	20.18± 0.82	19.11± 0.87	22.52± 0.9	21.58± 1.07	20.58± 1.37

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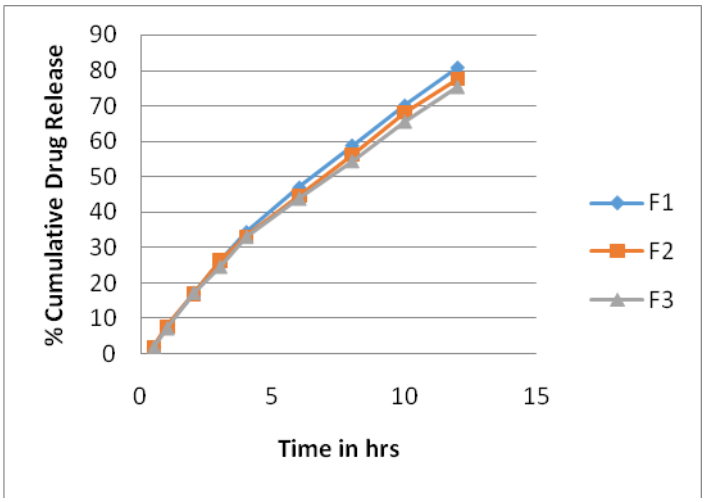
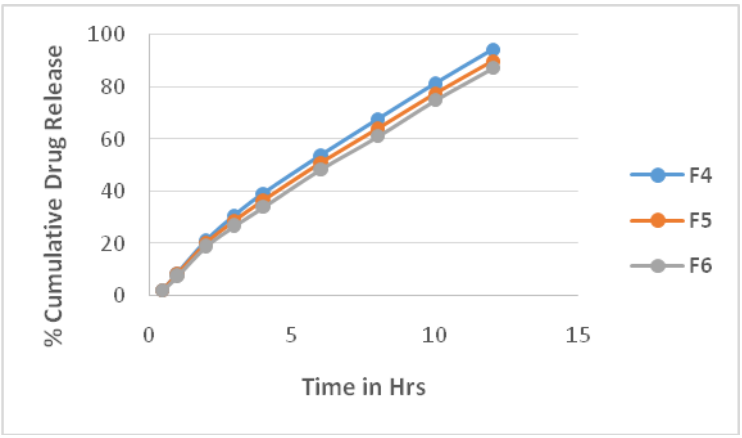
Dissolution data in phosphate buffer pH 6.8 (+ 250 mL of 0.2 M tri-sodium phosphate)										
4	**3**	26.25± 2.12	26.4±0.86	24.55± 1.57	30.96± 1.00	28.85± 1.27	26.93± 1.48	32.79± 1.12	30.88± 1.53	29.88± 1.53
5	**4**	34.5± 1.28	33.2±1.67	32.98± 1.56	39.27± 1.40	36.57± 1.11	34.09± 1.19	42.81± 1.80	39.12± 1.35	37.12± 1.35
6	**6**	457.06 ±1.87	44.6 ±1.78	43.79± 1.41	53.8± 1.88	50.95± 2.54	48.52± 1.99	56.96± 1.77	53.66± 1.57	50.52± 1.81
7	**8**	58.89± 1.51	56.22± 1.49	54.35± 0.7	67.66± 2.54	64.12± 1.89	61.15± 1.52	70.83± 1.28	66.03± 1.09	63.15± 1.52
8	**10**	70.18± 1.48	68.18±1.58	65.5± 1.97	81.29± 1.59	77.52± 2.08	74.90± 1.51	84.15± 1.04	80.02± 1.24	78.90± 1.51
9	**12**	80.87± 1.41	77.47± 0.85	75.27± 2.13	94.24± 1.57	89.9±1 .10	87.11± 1.59	97.02± 1.97	91.79± 1.43	90.12± 1.97



A



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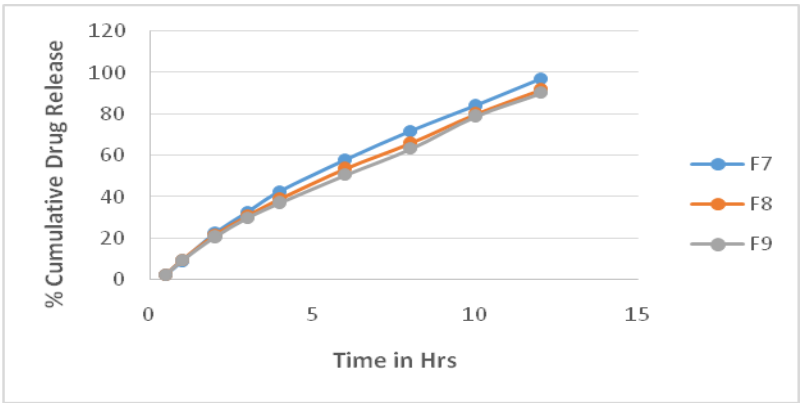


C

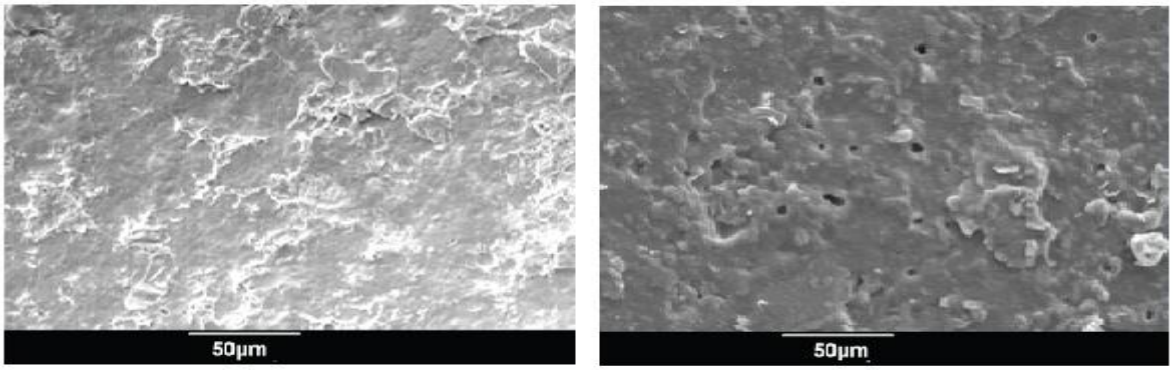
Figure: In-vitro release profile for vildagliptin A. Sodium Chloride (10 mg) B. Sodium Chloride (20 mg) C. Sodium Chloride (30 mg)

Model Fitting of *In-Vitro* Dissolution Data

The release pattern of all the formulations was studied using PCP Disso v2.0.8.5 software. All the formulations were fitted to zero order release, first order release, Higuchi matrix model, Hixson and Crowell powder dissolution model and Korsmeyer- peppas model. None of the formulations followed first-order kinetics, which was confirmed by the poor correlation coefficient values. All formulations best fitted both Higuchi matrix model (R^2 =0.9410 –0.9861) and Korsemeyer and Peppas equation (R2 =0.9502-0.9751). Osmotic tablet formulation of Vildagliptin coated with Cellulose acetate (F7) showed the best release pattern with highest R^2 value of 0.9861 in Higuchi matrix model.The value for diffusional exponent n was found between 0.5 (suggesting Fickian diffusion controlled drug release) and 1.0 (swelling-controlled drug release). For all formulations, the value of n was in the range 0.531-0.751indicating non-Fickian anomalous transport wherein the drug release mechanism was controlled by both diffusion and osmosis.

SEM Study

Optimum Tablet formulation batch(F7) were observed under Scanning electron microscope before and after dissolution (2 hrs). SEM analysis showed that there were no open pores on film surface before dissolution.While tablets kept for dissolution for 2 hours showed more number of pores on the coating film. The dissolution of pore forming agent-sorbitol present in the coating film resulted into formation of pores from where entrapped drug diffuses out slowly.



A. B.

Figure : SEM analysis of tablet formulation of VildagliptinA) before dissolution and B) after dissolution (2 hrs)

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Stability Testing of Optimized Formulation

Optimum tablet formulation F7 was evaluated for stability by storing at 40±2 ^{o}C /75±5% RH for 3 months. Tablets were observed for physical appearance, drug content and % cumulative drug release at the start of study, after one and three months of storage. Formulation was found to be stable at accelerated storage conditions.

Table 8: Stability evaluation of F7

	After storage at 40±2 ^{o}C /75±5% RH		
	0	**1 Month**	**3months**
Physical appearance	White	No change in physical Appearance	No change in physical Appearance
Drug content	99.62%	99.51%	99.40%
% Drug Released (After 12 hrs.)	97.32%	96.88 %	97.12%

CONCLUSIONS

- Controlled release osmotic tablets were prepared by wet granulation technique. Formulation optimization was done using 3^2 factorial design by varying concentration of osmogen-sodium chloride and HMPC EV 5. Nine trial formulations were prepared (F1 to F9) to study the effect of concentration of sodium chloride and HPMC EV5 on pre and post compression parameters. All formulation batches exhibited good flow behavior and compressibility. Core osmotic tablets were coated with coating solution. Formulation batches were evaluated for in-vitro drug release study in USP dissolution method for extended release tablet. In vitro drug release from batch F7 was found to be satisfactory. The drug release mechanism was controlled by both diffusion and osmosis. Formulation 7 was selected as optimum formulation for further osmotic tablet development.SEM study before and after dissolution revealed formation of pores at the surface of tablets.Stability was evaluated by storing tablet formulations at 40±2^{o}C /75±5% RH for 3 months. Evaluation test was performed in the beginning of study, after 1 and 3 months. The formulation F7 was found to be stable at accelerated conditions of temperature and humidity.

REFERENCES

1. Dhruv M. Formulation and evaluation of self pore forming osmotic tablets of glipizide IRJP 2012; 3 (4): 365-368.
2. Rao PB. Optimization and Development of Swellable Controlled Porosity Osmotic Pump Tablet for Theophylline Tropical Journal of Pharmaceutical Research, 2009; 8 (3): 247-255.
3. Sahoo CK. Formulation and Optimization of Controlled Porosity Osmotic Pump Tablets of Lamivudine using Sodium Chloride as Osmogen for the Treatment of AIDS Madridge J Nov Drug Res. 2(1): 94- 101.
4. Ganesh NS. Review on controlled porosity osmotic pump tablets and its basic components International Research Journal of Pharmaceutical and Biosciences (IRJPBS) 4 (3): 1- 14.

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Received 25 April 2021; Accepted 08 May 2021.

5. Fatema K, Shahi SR, Zaheer Z, Shaikh T. Formulation and Evaluation of Vildagliptin Immediate Release Tablet, World Journal of Pharmaceutical Research 2018; 7(5): 1214-1226.
6. Carstensen JT. Preformulation, In: Modern Pharmaceutics, Ed Banker GS, Rhodes CT, 4th Ed. Marcel Dekker, Inc. New York. 2002: 167-185.
7. Aulton ME. In: Pharmaceutics: The Science of Dosage Form Design, 2nd ed, Livingstone C. Elsevier Science Ltd., 2002:136-146.
8. Shrestha P, Bhandari SK, Islam SM, Reza MS, Adhikari S. Design and Development of Immediate and Sustained Release Tablets of Vildagliptin, Research Journal of Pharmaceutical, Biological and Chemical Sciences 2014; 5(4): 811-825
9. Costa P, Manuel J, Lobo S. Modeling and comparison of dissolution profiles. Eur J of Pharm Sci 2001; 13: 123–33.