World Journal of Pharmaceutical Science and Research

www.wjpsronline.com

Research Article

ISSN: 2583-6579

SJIF Impact Factor: 6.916

Year - 2026

Volume: 5; Issue: 5

Page: 413-432

FORMULATION AND EVALUATION OF VILDAGLIPTIN 100 MG SUSTAINED-RELEASE TABLETS BY USING POLYELECTROLYTE COMPLEX

S. S. Patil*, Vinod D. Usnale, Yogeshwar Baliram Bondge, C. V. Panchal, S. P. Kumbhar

Maharashtra College of Pharmacy, Nilanga, Dist. Latur, (M.S.)

Article Received: 6 March 2026 | | ***Article Revised: 28 March 2026*** | | ***Article Accepted: 17 April 2026***

***Corresponding Author: S. S. Patil**
Maharashtra College of Pharmacy, Nilanga, Dist. Latur, (M.S.)
DOI: https://doi.org/10.5281/zenodo.19917830

How to cite this Article: S. S. Patil, Vinod D. Usnale, Yogeshwar Baliram Bondge, C. V. Panchal, S. P. Kumbhar (2026) FORMULATION AND EVALUATION OF VILDAGLIPTIN 100 MG SUSTAINED-RELEASE TABLETS BY USING POLYELECTROLYTE COMPLEX. World Journal of Pharmaceutical Science and Research, 5(5), 413-432.

ABSTRACT

The goal of the current study was to Formulate Vildagliptin sustained release tablets by using Polyelectrolyte complex. Vildagliptin has very short half-life ie. (2–3 hours), therefore this medication is thought to be appropriate for sustained release tablet formulation, in order to extend its therapeutic effect. The Vildagliptin is a novel dipeptidyl peptidase-4 inhibitor class of oral anti-hyperglycemic medication. And this is drug of choice for the treatment of type 2 diabetes mellitus. The present study was carried out to evaluate the inter-polymer complex formed with Eudragit E100 and Eudragit L100 as a sustained release tablets for water soluble Vildagliptin. In this study six trials formulation was prepared .all the six trial contains equal amount of drug with IPE Complex and it Shows better results in all evaluation parameters amongst the all trials the trial F6 is better formulation and formulation F6 has better compatibility with all Excipients and has better dissolution profile as compared to all five (FI TO F5) formulations and formulation F6 has drug content uniformity is 99.21%, which was high as compared to all formulations and percentage drug release from polyelectrolyte complex is 98.87%. Among all the six trials with the physical mixtures, the one with the 1:1 ratios was found to be the best as compared to all other ratios and it is given controlled release profile as per USP limits.

KEYWORDS: Vildagliptin, Polyectrolyte Complex, Eudragit E100 and Eudragit L100, oral anti-hyperglycemic agent.

1.0. INTRODUCTION

1.1 Oral Drug Delivery

Oral drug delivery method is the most widely utilized routes for administration among all alternatives that have been explored for systemic delivery of drug via various pharmaceutical products of different dosage forms.[1,2,3,4,5] With many drugs, the basic goal is to achieve a steady state blood level that is therapeutically effective and non-toxic for an extended period of time. The design of proper dosage form is an important element to accomplish this goal. Sustained release, sustained action, prolonged action, controlled release, extended action, timed release and depot dosage form as term used to identify drug delivery system that are designed to achieve prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose. In the case of oral sustained released dosage form, an effect is for several hours depending upon residence time of formulation in the GIT.[5,6]

Conventional drug therapy requires periodic doses of therapeutic agents. These agents are formulated to produce maximum stability, activity and bioavailability. For most drugs, conventional methods of drug administration are effective, but some drugs are unstable or toxic and have narrow therapeutic ranges. Some drugs also possess solubility problems. In such cases, a method of continuous administration of therapeutic agent is desirable to maintain fixed plasma levels. To overcome these problems, controlled drug delivery systems were introduced three decades ago. These delivery systems have a number of advantages over traditional systems such as improved efficiency, reduced, toxicity, and improved patient convenience.[7,8]

Sustained release dosage forms: Any drug or dosage for modification that prolongs the Therapeutic activity of the drug. There lease of the drug is retarded for a delayed and prolonged period of time in the systemic circulation. Sustained release formulation maintains a uniform blood level of drug with better patient compliance as well as increased efficacy of drug.(9,10,11) Sustained release tablets are generally taken once or twice a day during a course of treatment whereas in conventional dosage forms there is need to take 3-4 times dosage in a day to achieve the same therapeutic action. The regular measurement structures are quickly supplanted by this novel's sustained discharge procedures. The terms Sustained Release, Delayed Release or Prolong Release formulations are utilized to recognize drug delivery systems that are intended to accomplish or expand therapeutic impact by ceaselessly discharging medicine over an all-encompassing period of time after administration of a unit dose.[12,13] Any drug or measurement structure adjustment that draws out the therapeutic action of the drug. The arrival of the drug is hindered for a postponed and delayed period of time in the fundamental circulation.

2.0 MATERIALSAND METHOD

Materials and Method

Wet granulation was used to prepare the SR tablets, with varying ratios of synthetic polymers. Granules were prepared, and their compressibility index, Hausner's ratio, bulk density, and tapped density were assessed. Utilized Statistical Analysis.[8,9] The vildagliptin and various polymers' individual and combined Fourier-transform infrared spectra demonstrate the medication's compatibility with excipients.

Vildagliptin was purchased from Enicar Pharma Ltd, Nagothane, Raigad. MCC, HPMC, Magnesium sterate, talc were used from Maharashtra college of Pharmacy, Nilanga.

Table no. 1: List of Excipients used in this thesis.

Material	Source	Use
Vildagliptin IP	Enicar Pharma	Biguanide antidiabetic
Eudragit E100 USP/NF/EP/JPE	Research Chem Lab, Mumbai	Controlled release polymer
Eudragit L100 USP/NF/EP/JPE	Research Chem. Lab	Controlled release polymer
Inter polyelectrolyte complex (IPEC)	Synthesized	Sustained release polymer
Isopropyl alcohol IP	Research Chem. Lab	Solvent
PVP – K 30 IP	Research Chem. Lab	Binder
Magnesium Stearate IP	Research Chem. Lab	Lubricant
Talc IP	Research Chem. Lab	Lubricant
Aerosil	Research Chem. Lab	Glident
MCC	Research Chem. Lab	Filler
HPMC	Research Chem. Lab	Polymer

3.0 PREPARATION OF SR TABLETS OF VILDAGLIPTIN BY USING POLYELECTROLYTE COMPLEX:

1. All the ingredients were accurately weighed.
2. All weighed ingredients sifted separately with appropriate sieve/mesh (#40).
3. Binder mixed with purified water at quantity sufficient. And prepare binder solution
4. This solution adds frequently in weighed drug and Excipients and make a damp mass.
5. Make the granules and Dry it.
6. This dried granules pass into sieve no. #10
7. Add it in lubricant and glidant passing from sieve no. #42
8. All the prepared granules fill in the container
9. Compressed the granules by Using 6 x3 mm Punch by using 10 station single rotary compression machine

3.1. FORMULATION TRIALS OF SR TABLETS

Table no. 2: Formulation trials F1 TO F3.

Ingredients	FORMULATION TRIALS		
	FI	F2	F3
	Qty. per tablet (mg)	Qty. per tablet (mg)	Qty. per tablet (mg)
Vildagliptin	100	100	100
Eudrajit E 100	60	100	75
Eudrajit L 100	100	60	75
HPMC	10	10	10
PVPK-30	08	08	08
MCC	12	12	22
Aerosil	4.5	4.5	4.5
Mg. Stearate	3.0	3.0	3.0
Talc	2.5	2.5	2.5
Total weight	300	300	300

Table no. 3: Formulation trials F4 TO F6.

Ingredients	FORMULATION TRIALS		
	F4	F5	F6
	Qty. per tablet (mg)	Qty. per tablet (mg)	Qty. per tablet (mg)
Vildagliptin	100	100	100
IPEC	50	85	100
HPMC	10	10	13
PVPK-30	08	08	08
MCC	122	87	65
Aerosil	4.5	4.5	8.5
Mg. Stearate	3.0	3.0	3.0

Talc	2.5	2.5	2.5
Total weight	300	300	300

4.0 Evaluations

4.1 RESULTS OF PRE-FORMULATION STUDIES

Table no. 4.Organoleptic properties of Vildagliptin

Property	**Observation**
Organoleptic	White, Crystalline, Hygroscopic powder which is Odorless and has bitter taste

4.1.2 Microscopy

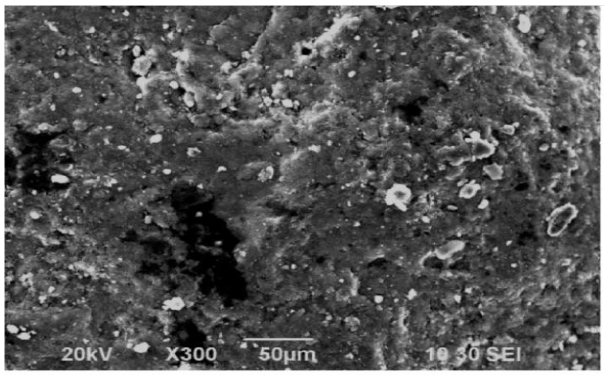

Fig. 1: Vildagliptin Microscopy at 100X.

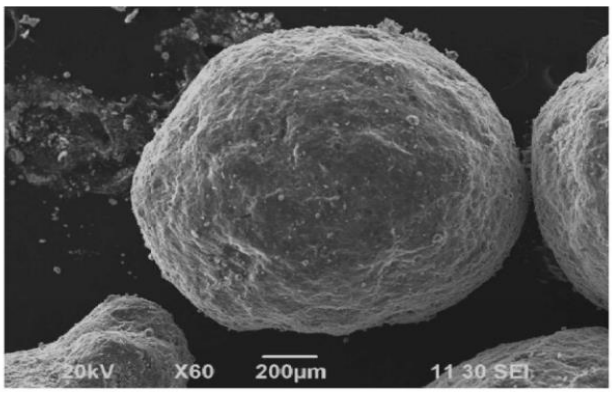

Fig. no. 2: Vildagliptin Microscopy at 400X.

Discussion: From the above figures we can conclude that the API is crystalline in nature.

Table no. 5: Solubility of Vildagliptin.

Solvent	**Solubility**
Water	Freely soluble
Ethanol (95%)	Slightly soluble
Acetone	Practically insoluble
Chloroform	Practically insoluble
Dichloromethane	Practically insoluble
Ether	Practically insoluble

Table no. 6 Melting point of Vildagliptin

Melting Point	**225^{0}C (222-226^{0}C)**

Discussion: As the melting point of the API was within the reported ranges, we concluded that the API was in its pure, metastable and pharmacologically active form.

Table no. 7: IR peaks of various functional groups of Vildagliptin.

Energy (cm-1)	Assignment
1630, 1565	N-H deformation and asymmetric NCN stretch
1470, 1440, 1410	CH3 asymmetric and symmetric deformations
1060, 940	C-N stretch and CH3 rock

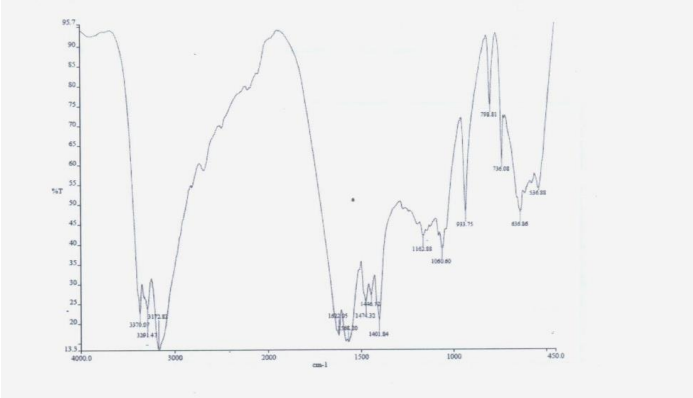

Fig. 3: IR spectrum of Vildagliptin.

Table no. 8: Bulk characterization of Vildagliptin.

LBD (g/ml)	TBD (g/ml)	Carrs index of compressibility (%)	Hausners ratio	Angle of repose (^{0})	Result
0.54	0.71	24.13	1.31	No flow through funnel	Passable flow

LBD = Loose Bulk Density TBD = Tapped Bulk Density

Discussion: The results showed that Vildagliptin had poor flow and compression properties.

Table no. 9: Standard calibration curve for Vildagliptin.

Sr. No.	Concentration (µg/ml)	Absorbance
0.	0	0
1.	1.00	0.150
2.	2.00	0.232
3.	3.00	0.372
4.	4.00	0.481
5.	5.00	0.582
6.	6.00	0.697
7.	7.00	0.823
8.	8.00	0.936

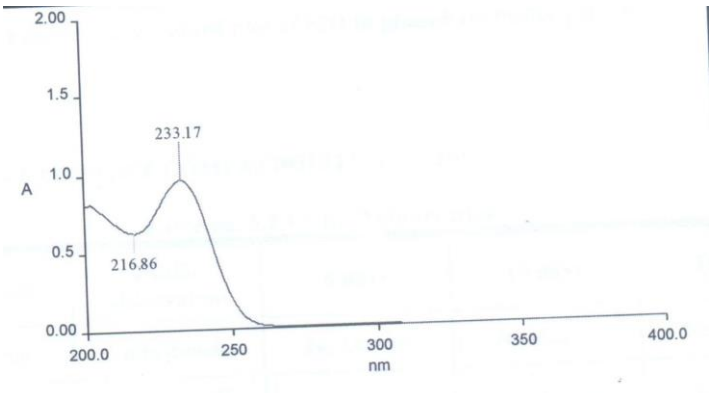

Fig. 4: The λmax of Vildagliptin.

Discussion: The λmax for MH was found to be 233nm

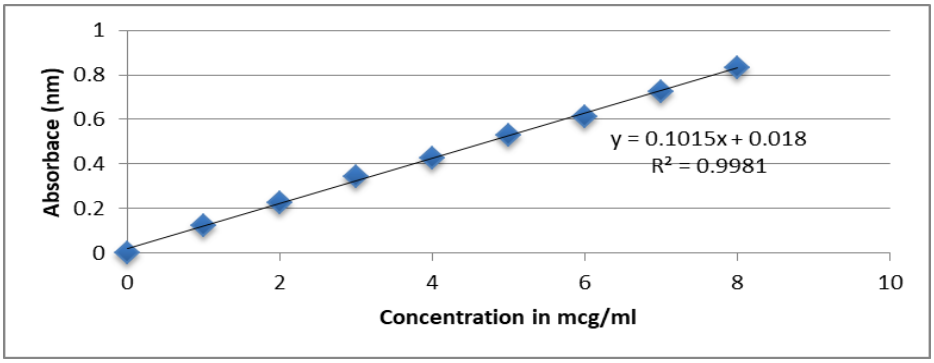

Fig. 5: Standard calibration plot of Vildagliptin in phosphate buffer pH 6.8.

4.2 DRUG-EXCIPIENT COMPATIBILITY TESTING

Table no. 10: drug-Excipients compatibility testing.

Ingredients	Initial observation	5 days	10 days	15 days
Vildagliptin	White Powder	No change	No change	No change
Vildagliptin+ Eudragit E100	White to off white powder	No change	No change	No change
Vildagliptin+ Eudragit L100	White powder	No change	No change	No change
Vildagliptin+ IPEC	Off white powder	No change	No change	No change
Vildagliptin+ Mg. Sterate	White power	No change	No change	No change
Vildagliptin+ Talc	White powder	No change	No change	No change
Vildagliptin+ HPMC	White powder	No change	No change	No change
Vildagliptin+ Aerosil	White powder	No change	No change	No change
Vildagliptin+ MCC	White powder	No change	No change	No change
Vildagliptin+ PVPK-30	Off white powder	No change	No change	No change

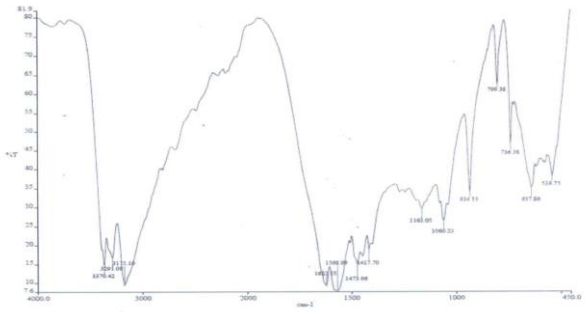

Fig. 6: IR spectrum of Vildagliptin+ Eudragit E100.

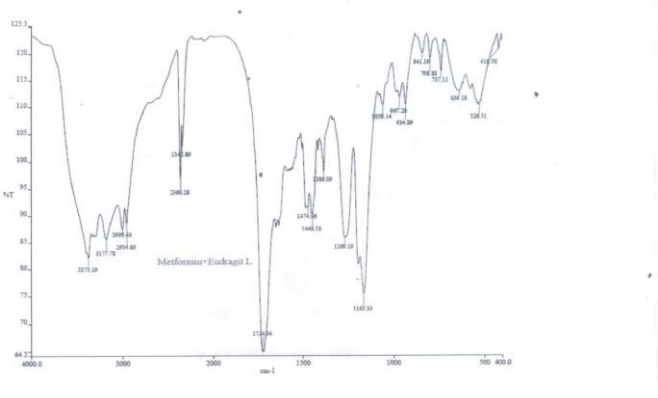

Fig. 7: IR spectrum of Vildagliptin+ Eudragit L100.

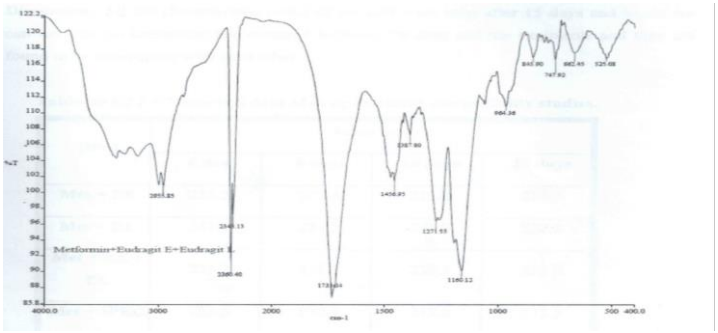

Fig. 8: IR spectrum of Vildagliptin+ Eudragit E100 + Eudragit L100.

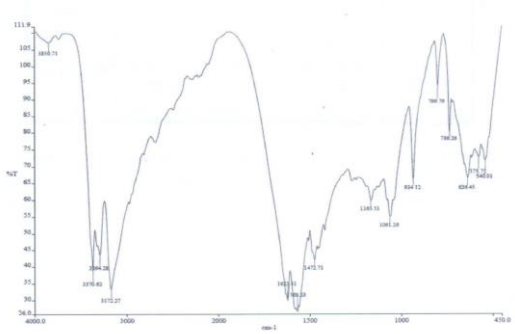

Fig. 9: IR spectrum of Vildagliptin+ IPEC.

Discussion: All the characteristic peaks of the API were seen after 15 days and hence we can say that no interaction has occurred between the drug and the excipients and they are found to be compatible with each other.

Table no. 11: UV spectral data of drug-excipient compatibility studies.

Drug	λmax (nm)			
	0 days	5 days	10 days	15 days
VILDA + EE	233.2	233.4	232.8	233.4
VILDA + EL	233.1	233.3	233.0	232.8
VILDA + EE + EL	233.2	232.8	233.5	233.0
ILDA + IPEC	233.2	232.7	233.0	233.3
VILDA + Mg. Stearate	233.4	233.3	232.8	233.4
VILDA + Talc	233.1	232.7	233.2	233.4
VILDA + HPMC	233.0	233.1	232.9	233.5

Discussion: The solution of the mixtures showed λmax at around 233 nm which indicates that no interaction has occurred among the drug and excipients and they are found to be compatible with each other.

4.3 TURBIDITY MEASUREMENTS

Table no. 12: Turbidity measurements.

Composition of mixture [EE/EL]	Relative turbidity EE added to EL	Relative turbidity EL added to EE
1:3 (0.33)	0.12	0.11
1:2 (0.5)	0.21	0.19
1:1.5 (0.67)	0.53	0.60
1:1 (1)	1	1
1:0.8 (1.25)	0.60	0.58
1:0.5 (2)	0.11	0.10
1:0.3 (3)	0.09	0.09

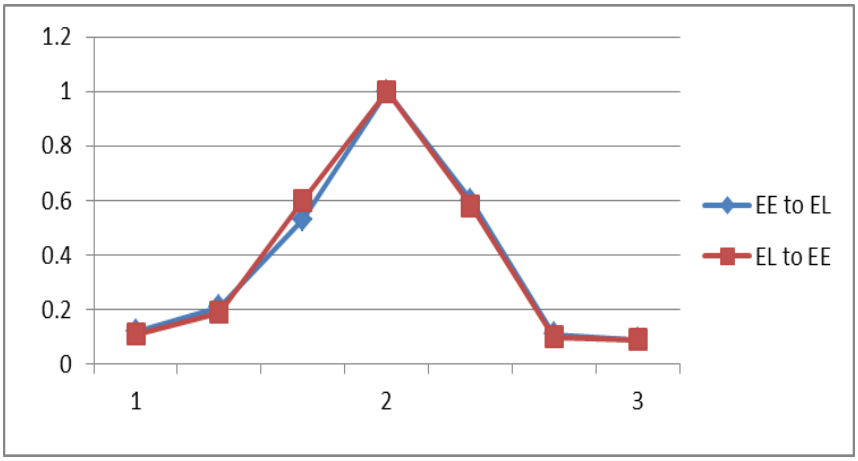

Fig. 10: Plot of relative turbidity.

4.3.1 Discussion: Maximum turbidity was seen at 1:1 ratio which indicates maximum formation of the IPEC as compared to the other molar weight rations. The turbidity was measured at pH 6 at which the two polymers are partially ionized. The addition of an excess amount of EE again led to a drop in the turbidity value due to segregation of the formed IPEC. The observed binding molar ratio corresponds to the stoichemestry of the obtained product. The order of mixing also plays a role in the formation of the IPEC. Hence, the turbidity measurements were done when EE was added to EL and EL added to EE. We found that the order of mixing does not play a major role as the two curves overlap.

4.4 VISCOCITY MEASUREMENTS

Table no. 13: Viscosity measurements.

Composition of mixture [EE/EL]	Specific viscosity
1:3 (0.33)	4.57
1:2 (0.5)	3.23
1:1.5 (0.67)	2.83
1:1 (1)	2.65
1:0.8 (1.25)	5.96
1:0.5 (2)	8.78
1:0.3 (3)	10.32

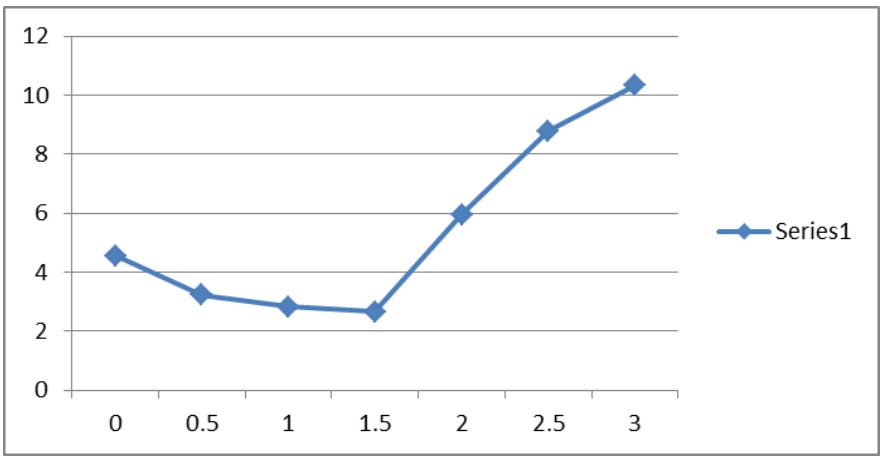

Fig. 11: Plot of Viscosity measurements.

4.4.1 Discussion: Generally when EE or EL is added alone there is an increase in specific viscocity of the solution with an increase of the polymer concentration. Therefore, the decrease of viscosity observed in the EE-EL mixture system showed that the IPEC was formed in the investigated medium and was removed by centrifugation. When the mixture of the two polymers becomes equimolar, a minimum in the curve is seen.

4.5 FTIR spectra results

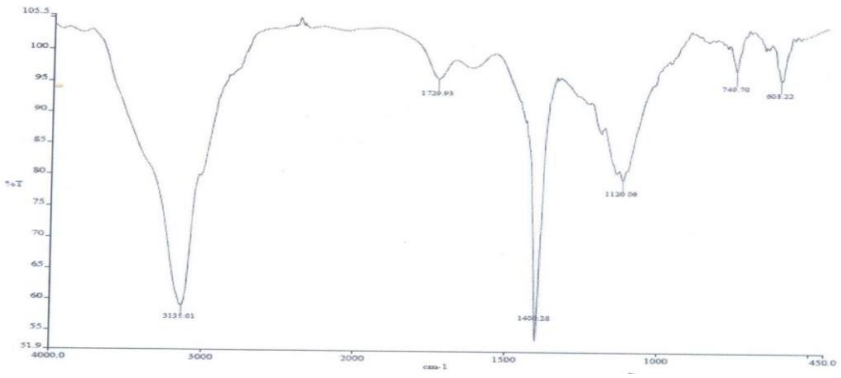

Fig. 12: FT-IR spectra of Eudragit E100.

The characteristic bands of the ester groups at 1150-1190, 1240 and 1270 cm^{-1}, as well as the C = O ester vibration at 1730 cm^{-1}. In addition, CH_x vibrations can be discerned at 1385, 1450 – 1490. The absorptions at 2770 and 3020 cm^{-1} can be assigned to the dimethylamino groups.

4.5.1 Eudragit L100\Ā2

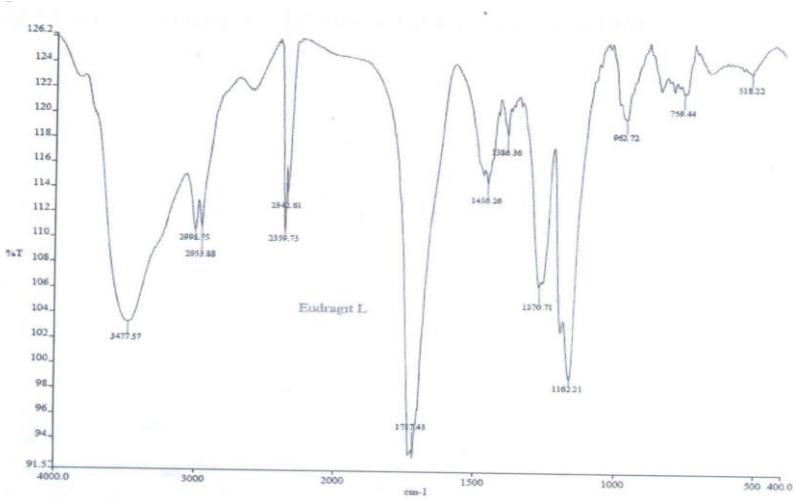

Fig. 13: FT-IR spectra of Eudragit L100.

The characteristic bands of the C=O vibrations of the carboxylic acid groups at 1705 cm-1 and f the esterified carboxyl groups at 1730 cm-1, as well as further ester vibrations at 1150 – 1160, 1190 – 1195 and 1250 – 1275 cm-1. The wide absorption range of the associated OH groups between 2500 and 3500 cm-1 is superimposed by CHX vibrations at 2900-3000 cm-1. Further CHX vibrations canbe discerned at 1385 – 1390, 1450 and 1485 cm-1. The more intensive C=O band of the carboxylic acid groups at 1705 cm-1 shows that EUDRAGIT® L 100 has a higher methacrylic acid content.

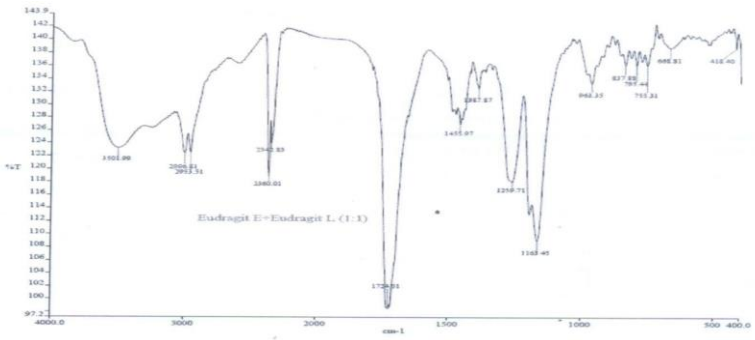

Fig. 14: FTIR Spectra of Physical mixture of Eudragit E100 and Eudragit L100 (1:1).

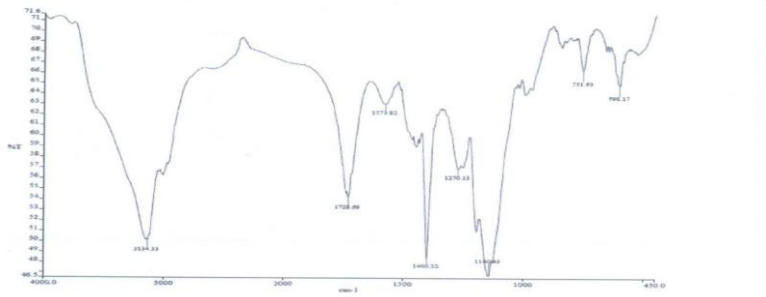

Fig. 15: FIIR Spectra of IPEC.

The FTIR spectra of the solid complex showed some differences as compared to those of a physical mixture of EL and EE at a molar weight ratio of 1:1. A band appears at 1520 cm-1 which might be assigned to the absorption band of carboxylate groups that form the ionic bonds with protonated dimethylamino groups of EE. On the other hand, peak broadening at approximately 2548 cm-1, might be assigned to the polymer salt absorption band which was brought about by the interaction of the dimethylamino groups of EE with the carboxyl groups of EL. The ratio of the bands at 2773 and 2824 cm-1 significantly changed. This indicates a difference in the amount of protonated and non-protonated dimethylamino groups. Changes in the hydroxyl stretching region are observed as well.

4.6 DEGREE OF SWELLING OF POLYMERIC MATRIX

Table No. 14: Swelling index.

Time (hrs)	Degree of swelling (H%) of IPEC	Degree of swelling (H%) of physical mixture
0	0	0
0.5	200	150
1	275	175
1.5	300	200
2	345	225
2.5	350	235
3	325	250
4	400	300
5	440	305
6	442	310
7	449	300
8	449	295
9	425	300
10	375	275
11	350	265
12	345	250

4.6.1 Discussion: The degree of swelling of the IPEC was found to be better compared to the physical mixture because in the physical mixture each component is acting individually and there is no interaction between the polymers.

4.7 EVALUATION OF THE BLEND AND THE SUSTAINED RELEASE VILDAGLIPTIN TABLETS

Table no. 15: Bulk characterizations of granules.

Formulation	LBD (g/ml)	TBD (g/ml)	Hausners ration	Carrs index of compressibility (%)	Angle of repose(^{0})
F-1	0.49	0.64	1.30	22.92	32.54
F-2	0.49	0.63	1.28	21.97	30.95
F-3	0.50	0.63	1.25	20.86	31.28
F-4	0.50	0.64	1.27	21.54	29.47
F-5	0.49	0.63	1.28	21.86	30.67
F-6	0.47	0.60	1.26	21.66	27.81

4.7.1 Discussion: From the values obtained, we found that the tablet blend of all the trials had good flow and compression properties.

4.8 Physicochemical properties of tablets

Table no. 16: Physicochemical properties of tablets.

Formulation	Thickness (mm)	Hardness (Kg/cm^2)	Average Weight (mg)	Friability (%)	Drug content (%)
T-1	8.47	07	1010	0.68	101.13
T-2	8.83	08	1015	0.59	98.21
T-3	8.07	08	1012	0.45	101.57
T-4	6.63	07	610	0.61	102.60
T-5	6.48	07	807	0.62	98.36
T-6	8.94	08	1012	0.55	99.21
Marketed	6.08	09	716	0.43	99

4.9 IN-VITRO DISSOLUTION TEST

Table no. 17: in-vitro dissolution test results.

Time in Hrs.	Percentage drug release					
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
0	0	0	0	0	0	0
1	20.57	21.87	20.67	38.67	22.67	33.42
2	30.62	44.32	32.54	45.27	48.32	39.67
3	49.5	59.81	45.68	60.91	52.8	48.38
4	53.37	60.18	48.57	61.1	54.32	52.88
5	58.15	61.23	58.48	62.32	58.32	63.53
6	60.82	63.85	63.89	63.81	60.82	78.96
7	62.94	71.22	69.98	72.14	75.82	81.48
8	67.63	73.06	79.83	74.53	84.83	83.67
9	71.76	78.032	84.32	78.33	87.32	85.72
10	77.12	80.31	88.84	87.33	98.32	87.37
11	85.96	89.13	93.28	90.27	99.05	94.32
12	94.45	97.42	97.32	96.91	----	98.87

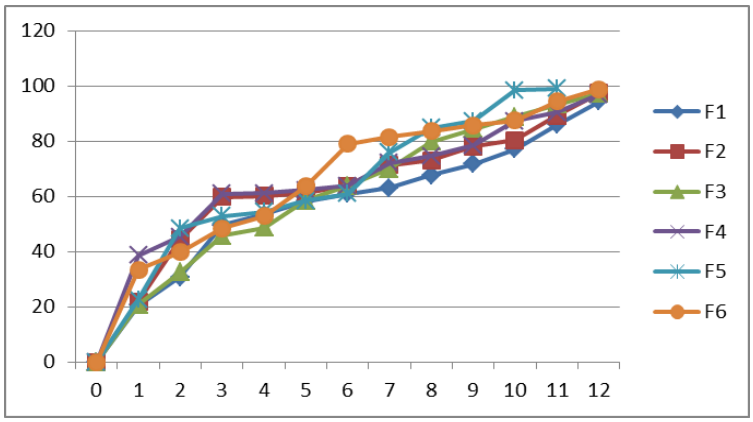

Fig. 16: Comparative plot for dissolution of all formulations.

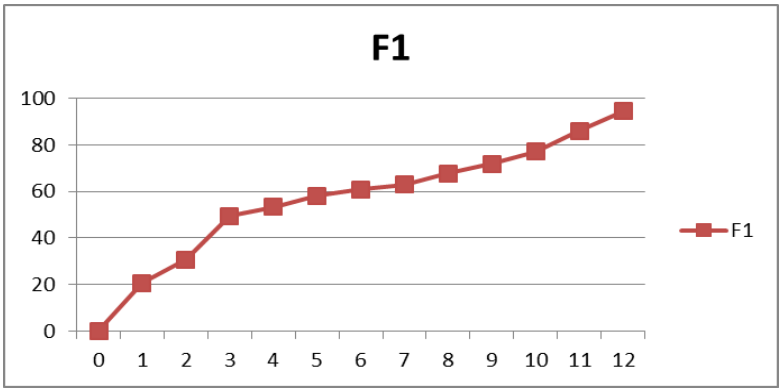

Fig. 17: In vitro release data of Vildagliptin loaded sustained release tablets (F1).

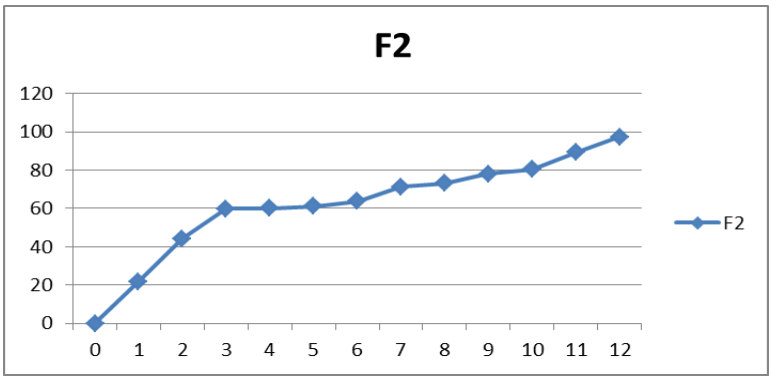

Fig. 18: In vitro release data of Vildagliptin loaded sustained release tablets (F2).

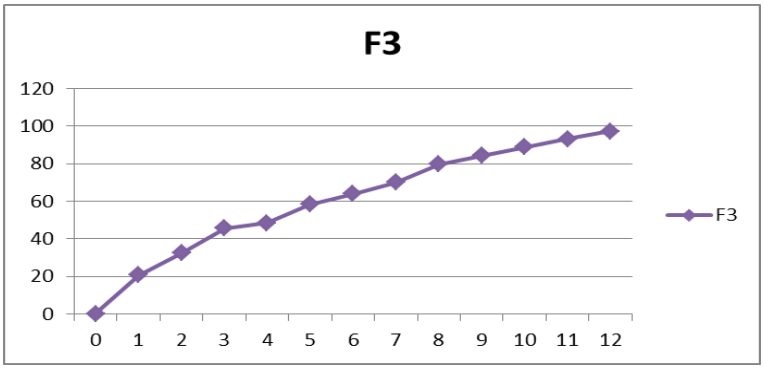

Fig. 19: In vitro release data of Vildagliptin loaded sustained release tablets (F3).

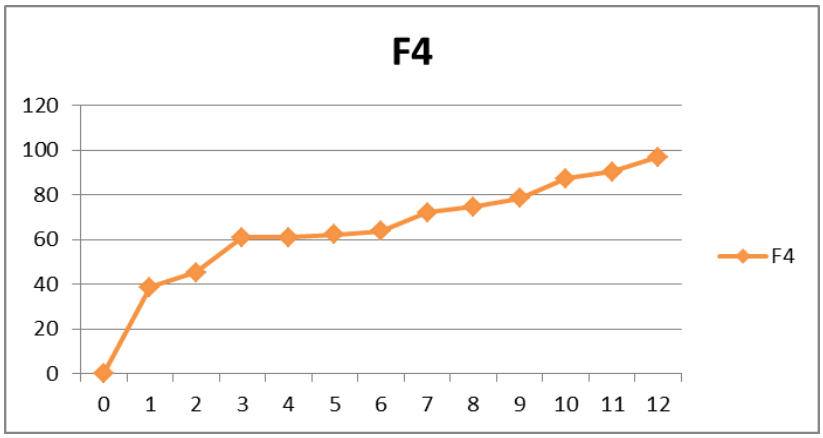

Fig. 20: In vitro release data of Vildagliptin loaded sustained release tablets (F4).

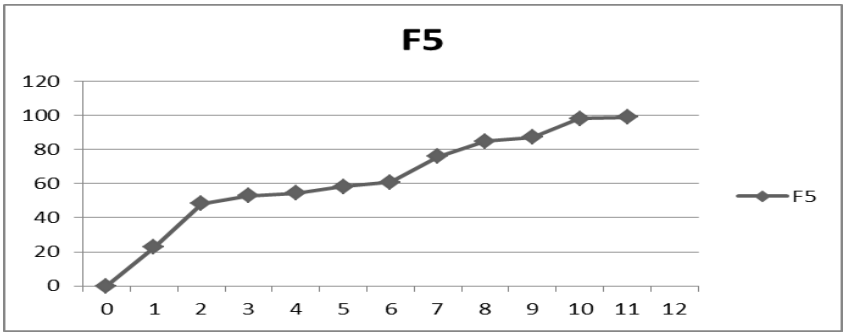

Fig. 21: In vitro release data of Vildagliptin loaded sustained release tablets (F5).

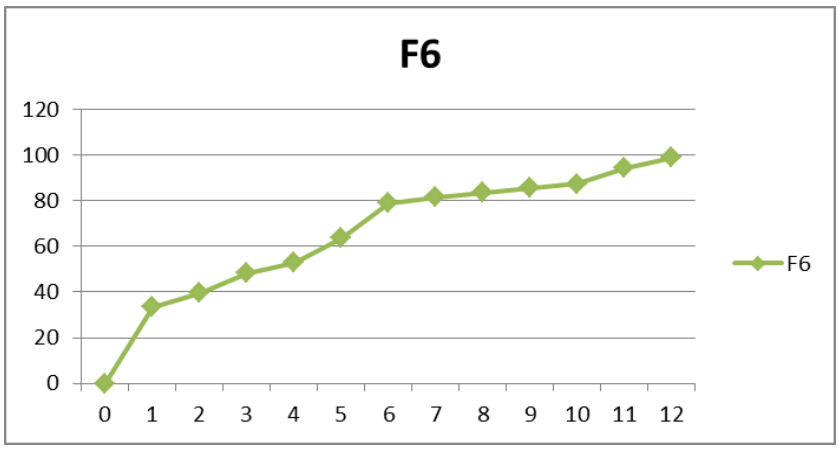

Fig. 22: In vitro release data of Vildagliptin loaded sustained release tablets (F6).

Table no. 18: In vitro release data of Vildagliptin loaded marketed Sustained release tablets.

Time in hrs.	In vitro release
	Tab 1(n=3)
0	0
1	20.32±0.055
2	27.42±0.034
3	36.39±0.034
4	49.67±0.061
5	55.37±0.086
6	65.73±0.013
7	74.53±0.040

8	83.47±0.096
9	89.67±0.083
10	93.58±0.056
11	96.79±0.061
12	99.32±0.083

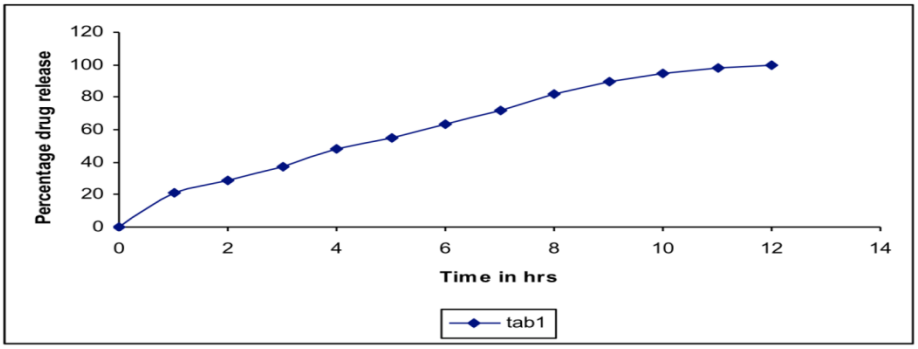

Figure 23: in vitro release data of Vildagliptin loaded marketed preparation.

4.10 Polyelecrtolyte complex of Vildagliptin

Vildagliptin was found to be white, crystalline, hygroscopic powder which is odorless and having a bitter taste.

- Microscopic studies suggested that Vildagliptin has an average particle size of 2.2µm and existed in two forms i.e. Fibrous and Flaky.
- The solubility studies of Vildagliptin showed that it is freely soluble in water, slightly soluble in ethanol and insoluble in acetone, chloroform and ether.
- The melting point of Vildagliptin was found to be 225^0C, which is in good correlation with the standard (222-226^0C).
- IR spectrum of Vildagliptin showed principal peaks at 1630, 1565, 1440 and 1060 indicating presence of N-H, NCN, CH3 and C-N groups respectively.
- The values obtained from Carr's index of compressibility, Hausners ratio and angle of repose indicated that Vildagliptin had poor flow and compression characteristics and hence not a suitable candidate for direct compression.
- UV spectrum of Vildagliptin exhibits maximum absorption at 233.0 nm
- A linear relationship was obtained in Beer-Lambert's plot of Vildagliptin having degree of correlation (r^2 – 0.9978) in pH 6.8 phosphate buffer.
- Drug – Excipients compatibility study showed no interaction between Vildagliptin and selected Excipients as indicated by the IR and UV spectra.

4.11Polymers

- Interpolylectrolyte complex (IPEC) formed by mixing different concentrations of Eudragit E100 and Eudragit L100 was used as the sustained release polymer
- Tubidimetric measurements showed maximum turbidity at the unit molecular weight ratio of 1:1 (EE/EL) which indicated good formation of IPEC. Viscosity measurements indicated a decrease in viscosity at the molar weight ration of 1:1 which showed that the IPEC was formed in the investigated medium

- FT-IR spectra indicated charges in the structure of the IPEC as compared to the physical mixture of the two Eudragits.
- The IPEC complex showed better swelling properties compared to the physical mixture because in case of the physical mixture the polymers are acting individually and no inter polymer interaction occurs.

4.12 Vildagliptin tablets

- The tablets were prepared by wet granulation technique.
- The granules were evaluated for angle of repose, Hausner ratio and Carr's index of compressibility. The values indicated good flow and compression characteristics contradictory to that seen with Vildagliptin alone.
- All the formulations were evaluated for thickness, hardness, friability, weight variation and drug content. The formulations were found to be within the prescribed limits.
- The drug release kinetics could not be predicted by a single release model and the drug release appeared to be a complex mechanism of swelling, diffusion and erosion.

4.13 In-vitro drug release:

- The IPEC showed good sustained release as compared to be physical mixture of the two polymers.
- The IPEC formed at molar weight ration of 1:1 showed sustained release in accordance with the USP ranges as compared to other rations like 1:3, 1:2, 1:0:5.

Among the trials with the physical mixtures, the one with the 1:1 ratios was found to be the best compared to other ratios and is give controlled release as per USP limits.

Both F6 and Marketed formulation showed first order kinetics which indicated that the drug release was dependant on concentration. Both formulations complied with Higuchi model which indicated that drug release was by diffusion form the polymeric matrix and they also complied with the Korsemeyers-peppas model which showed that the release was by diffusion, swelling and erosion from the polymeric matrix. The drug release kinetics could not be predicted by a single release model and the drug release appeared to be a complex mechanism of swelling, diffusion and erosion.

5.0 CONCLUSION

- The present study was carried out to evaluate the inter-polymer complex formed with Eudragit E100 and Eudragit L100 as a sustained release matrix for water soluble Vildagliptin.
- Results of the present study demonstrated that tablets formulated with the polyion complex sustain the release more than that of physical mixture (1:1) of the two polymers.
- The polyion complex SR tablet is a promising approach to achieve appropriate sustained release dosage forms.
- Further research needs to be conducted to be conducted to access different agents capable of forming inter polymer complex and their utility as sustained release polymers.
- From all above six trials formulation F6.contains equal amount of drug with IPEC Complex and it shows better results in all evaluation parameters hence F6 is better formulation.and formulation F6 has better compatibility with all Excipients and has better dissolution profile as compared to all formulation and drug content uniformity is 99.21 which was high as compared to all formulations and percentage drug release is 98.87%
- The IPEC showed good sustained release as compared to be physical mixture of the two polymers.

- The IPEC formed at molar weight ration of 1:1 showed sustained release in accordance with the USP ranges as compared to other rations like 1:3, 1:2, 1:0:5.

Among the trials with the physical mixtures, the one with the 1:1 ratios was found to be the best compared to other ratios and is give controlled release as per USP limits.

Both F6 and Marketed formulation showed first order kinetics which indicated that the drug release was dependant on concentration. Both formulations complied with Higuchi model which indicated that drug release was by diffusion form the polymeric matrix and they also complied with the Korsemeyers-peppas model which showed that the release was by diffusion, swelling and erosion from the polymeric matrix. The drug release kinetics could not be predicted by a single release model and the drug release appeared to be a complex mechanism of swelling, diffusion and erosion.

6.0 REFERENCES

1. Lankalapalli S, Kolapalli RM.Polyelectrolyte complexes: A review of their applicability in drug delivery technology.Indian J.Pharm. Sci, 2009; 71(5): 481-487.
2. Narayan B, Gunn J and Zhang M.Chitosan-based hydrogels for controlled, localized drug delivery.Adv.Drug Deliv. Rev.(2009), doi: 10.1016/j.addr.2009.07.019.
3. Kopecek J. Hydrogel biomaterial: A smart future?.Biomaterials, 2007; 44(7): 1-8.
4. Geever L M, Cooney CC, Lyons JG, Kenndy JE, Nugent MJD, et al. Characterisation and controlled drug release from novel drug-loaded hydrogels. European journal of pharmaceutics and Biopharmaceutics, 2008; 69: 1157-1159.
5. Jeong SH, Fu Y and Park K. Hydrogls for oral administration. Department of pharmaceutics and biomedical engineering, Purdue Univerity, West Lafayette, Indiana, U. S.A, 195-200.
6. Chien-Chi L and Andrew TM.Hydrogels in controlled release formulations: Network design and mathematical modeling. Advance drug delivery reviews, 2006; 58: 1379-1408.
7. Kalpana R, Kamath and Park K. Biodegradable hydrogels in drug delivery. Advanced drug delivery reviews, 1993; 11: 59-84.
8. Sophie R, Tomme V, Storm G and Hennink WE. Insitu gelling hydrogels for pharmaceutical and biomedical applications.International Journal of Pharmceutics, 2008; 355: 1-18.
9. Gariepy ER and Leroux JC. Insitu-forming hydrogels: review of temperature-sensitive systems. European Journal of Pharmaceutics and Biopharmaceutics, 2004; 58: 409-426.
10. Kovacevic D, Borkovic S, Pozar J. The influence of ionic strength electrolyte type and preparation procedure on formation of weak polyelectrolyte complex. Colloids Surf, 2007; 302: 107-112.
11. Yin YJ, Yao KD, Cheng GX and Ma JB.Properties of polyelectrolyte complex films of chitosan and gelatin.Polymer International, 1999; 48(6): 429-432.
12. Hugerth A, Ninus CL, Sundelof LO.The effect of charge density and conformation on the polyelectrolyte complex formation between carrageenan and chitosan. Carbohydr Polym, 1997; 34: 149-156.
13. Biesheuvel PM, Martien A and Stuart C. Cylinderical cell model for the electrostatic free energy of polyelectrolyte complexes. Langmuir, 2004; 20(11): 4764-4770.
14. Kikuchi Y, Kubota N. Structure properties and Na^+ transport membrane of polyelectrolyte complexes consisting of glycol chitosan and poly (vinyl sulfate). Bull Chem Soc. Japan, 1987; 60: 375.

15. Smolen VF, Hahman DE. A water membrane hypothesis behavior of hydrated polycation-polyanion salt complexed membranes as appeared lipoidal barriers to solute transport. J Colloid Interface Sci., 1973; 42: 70-78.
16. Mark HF, Bikales NM, Overberger CG, Menges G. Encyclopedia of polymer science. Vol. II, 2nd ed., John Wiley & Sons (NY): A Willey Interscience Publishers: 739.
17. Dumitriu S, Chornet E. Inclusion and release of proteins from polysaccharide based polyion complexes. Adv Drug Del Rev, 1998; 31: 223-246.
18. Bhise KS, Dhumal RS, Chauhan B, Paradkar A, Kadam SS.Effect of oppositely charged polymer and dissolution medium on swelling, erosion and drug release from chitosan matrices.*AAPS* Pharm Sci Tech, 2007; 8(2).
19. Berger J, Reist M, Mayer JM, Felt O, Gurny R. Structure and interactions in chitosan hydrogels formed by complexation or aggregation for biomedical applications. Eur J Pharm Biopharm, 2004; 57: 35-52.
20. Fini A and Orienti I. The role of chitosan in drug delivery current and potential applications. Am J. Drug Deliv, 2003; 1(1): 43-59.
21. Becheran-Maron L, Peniche C, Arguelles-Monal W. Study of the interpolyelectrolyte reaction between chitosan and alginate: influence of alginate composition and chitosan molecular weight.Int J Bio Macromol, 2004; 34: 127-133.
22. Gardlund L, Wagberg L, Norgren M. New insights into the structure of polyelectrolyte complexes. J Colloid Interface Sci., 2007; 312: 237-246.
23. Gotoh T, Matsushima K and Kikuchi KI. Preparation of alginate-chitosan hybrid gel beads and adsorption of divalent metal ions. Chemosphere; 2004; 55: 135-140.
24. Gomez-Burgaz M, Garcia-Ochoa and Torrado-Santiago. Chitosan- carboxy methyl cellulose inter polymer complexes for gastric-specific delivery of clarithromycin. International journal of pharmaceutics, 2008; 359: 135-143.
25. Hu Y, Jiang X, Ding Y, Ge H, Yuan Y, Yang C.Synthesis and characterization of chitosan-poly (acrylic acid) nanoparticles.Biomaterials, 2002; 23: 3193-3201.
26. Becheran-Maron L, Peniche C, Arguelles-Monal W. Study of the inter polyelectrolyte reaction between chitosan and alginate: influence of alginate composition and chitosan molecular weight.Int J Bio Macromol, 2004; 34: 127-133.
27. Costa P, Lobo JM.Review – modeling and comparison of diffusion profiles.Eur J Pharm Sci., 2001; 13: 123-133.
28. Rao NSN and Murthy NS. Applied statistics in health sciences. 1st edn, 2008; 158-172.
29. Mishra B, Bansal A and Sankar C. Development and invitro evaluation of hydrophilic matrix tablets of diltiazem HCl. Acta Pharmaceutica Turcica, 2005; 47: 115-126.
30. Tapia C, Escobar Z, Costa E, Sagar HJ, Valenzuela F, Basualto C et al. Comparative studies on polyelectrolyte complexes and mixtures of chitosan-alginate and chitosan-carrageenan as prolonged diltiazem clorhydrate release systems. Eur J Pharm Biopharm, 2004; 57: 65-75.
31. Bhaskaran S. Preparation and evaluation of alginate-chitosan beads. Indian J Pharm Sci., 2002; 389-391.
32. Park JH, Saravanakumar G, Kim K and Kwon IC. Targeted delivery of low molecular drugs using chitosan and its derivatives. Adv. Drug Deliv. Rev, 2009. doi: 10.1016/j.addr.2009.10.003.
33. George M, Abraham TE. Polyionic hydrocolloids for the intestinal delivery of protein drugs: alginate and chitosan – a review. J Control Rel, 2006; 114: 1-14.

34. Amal Ei-Kamel, Sokar M, Naggar V and Gamal AS. Chitosan and sodium alginate-based bioadhesive veginal tablets. AAPS Pharm Sci, 2002; 4(4): 1-7.
35. Fukuda H and Kikuchi Y.Polyelectrolyte complexes of chitosan with sodium carboxymethyldextran. Bulletin of the Chemical Society of Japan, 1978; 51(4): 1142-1144.
36. Pasparakis G, Bouropoulos N. Swelling studies and *in vitro* release of verapamil from calcium alginate and calcium alginate-chitosan beads.Int J Pharm, 2006; 323: 34-42.
37. Sankalia MG, Mashru RC, Sankalia JM, Sutariya VB. Reversed chitosan-alginate polyelectrolyte complex for stability improvement of alpha-amylase: optimization and physiochemical characterization. Eur J Pharm Biopharm, 2007; 65: 215-232.
38. Bhise KS, Vidhate V, Nangude T and Bora D. Enteric coated tablets of drug loaded chitosan microspheres for colon specific drug delivery system. Asian Journal of Pharmaceutics; 2007; 1(4): 202-207.
39. Hugo EA, Ofelia SC, Humberto VT, Eduardo JVC and Consuelo LC. Determination of gum Arabic-chitosan interactions by fourier transform infrared spectroscopy and characterization of the microstructure and rheological features of their coacervates. Carbohydrate Polymers, 2009. doi:10.1016/j.carbopol.2009.08.040.
40. Moustafine RI, Evgeniya BM, Liliya FS, Vera AK and Guy VDM. European Journal of Pharmaceutics and Biopharmaceutics; 2008; 70: 215-225.
41. Gaserod O, Smidsrod O, Skjak-Braek G. Microcapsules of alginate-chitosan-I: a quantitative study of the interaction between alginate and chitosan.Biomaterials, 1998; 19: 1815-1825.
42. Sipahigil O, Dortunc B. Preparation and *in vitro* evaluation of verapamil HCl and ibuprofen containing carageenan beads.Int J Pharm, 2001; 228: 119-128.
43. Kilicarslan M, Baykara T. The effect of the drug/ polymer ratio on the properties of the verapamil HCl loaded microspheres. Int J Pharm, 2003; 252: 99-109.
44. Shu XZ, Zhu KJ. The release behavior of brilliant blue from calcium-alginate gel beads coated by chitosan: the preparation method effect. Eur J Pharm Biopharm, 2002; 53: 193-201.
45. Mohammad RA, Assal MMS, Nasser M, Sideh A, Fatemeh A et al. Preparation and characterization of insulin nanoparticals using chitosan and Arabic gum with ionic gelation method. Nanomedicine:NBM, 2009 ;xx: 1-6,doi:10.1016/j.nano.2009.04.007.
46. Meshali MM and Gabr KE. Effect of Interpolyelectrolyte complex formation of chitosan with pectin or acacia on the release behaviour of chlorpromazine HCl. International Journal of pharmaceutics, 1993; 89(3): 177-181.
47. Chang KLB and Lin J. Swelling behavior and the release of protein from chitosan-pectin composite particles. Carbohydrate Polymer, 2000; 43(2): 163-169.
48. Piyakulawat P, Praphairaksit N, Chantarasiri N, Muangsin N. Preparation and evaluation of chitosan/ carrageenan beads for controlled release of sodium diclofenac. *AAPS* Pharm Sci Tech, 2007; 8(4).
49. Anil AK, Stevens WF. Chitosan-alginate multilayer beads for controlled release of ampicillin.Int J Pharm, 2005; 290: 45-54.
50. Liao I, Andrew CA, Evelyn KF, Leong KW. Controlled release from fibers of polyelectrolyte complexes. J Control Rel, 2005; 104: 347-358.
51. Mistumata T, Suemitsu Y, Fujii K, Fujii T, Taniguchi T, Koyama K. pH response of chitosan, κ-carrageenan, carboxymethyl cellulose sodium salt complex hydrogels. Polymer, 2003; 44:7103-7111.

52. Wang L, Khor E, Lim LY. Chitosan-alginate-$CaCl_2$ system for membrane coat application. J Pharm Sci., 2001; 90(8): 1134-1142.
53. Mladenovska K, Raicki RS, Janevik EI, Ristoski T, Pavlova MJ, Kavrakovski Z et al.Colon-specific delivery of 5-aminosalicylic acid from chitosan-Ca-alginate microparticles.Int J Pharm, 2007; 342: 124-136.
54. Jianlong W, Yi Q. Microbial degradation of 4-chlorophenol by microorganisms entrapped in carrageenan-chitosan gels. Chemosphere, 1999; 38(13): 3109-3117.
55. Shiqu Y, Wang C, Liu X and Tong Z. Deposition temperature effect on release of indomethacin microcrystals from microcapsules of layer-by-layer assembled chitosan and alginate multilayer films. Journal of Controlled Release, 2005; 106: 319-328.
56. Qi W, Ma J, Yu W, Xie Y, Wang W, Ma X.Behavior of microbial growth and metabolism in alginate-chitosan-alginate (ACA) microcapsule.Enzyme Microb Tech, 2006; 38: 697-704.
57. Aral C, Akbuga J.Alternative approach to the preparation of chitosan beads.Int J Pharm. 1998; 168: 9-15.
58. Douglas KL, Piccirilla CA, Tabrizian M.Effects of alginate inclusion on the vector properties of chitosan-based nanoparticles.J Controll Rel, 2006; 115: 354-361.
59. Park SH, Chun MK, Choi HK. Preparation of an extended-release matrix tablet using chitosan/ carbopol interpolymer complex.Int J Pharm, 2008; 347: 39-44.
60. Hu Y, Jiang X, Ding Y, Ge H, Yuan Y, Yang C.Synthesis and characterization of chitosan-poly (acrylic acid) nanoparticles.Biomaterials, 2002; 23: 3193-3201.
61. Sittinger M, Lukanoff B, Burmester GR, Dautzenberg H.Encapsulation of artificial tissues in polyelectrolyte complex: preliminary studies.Biomaterials, 1996; 17: 1049-1051.
62. Vasiliu S, Popa M, Rinaudo M. Polyelectrolyte capsules made of two biocompatible natural polymers. Eur Poly J., 2005; 41: 923-932.
63. Halder A, Maiti S and Sa. B. Entrapment efficiency and release charecterstics of polyethyleneimine treated or untreated alginate beads loaded with propanolol-resin complex. International Journal of Pharmaceutics, 2005; 302: 84-94.
64. Martin L, Wilson CG, Koosha F and Uchegbu IF. Sustained buccal delivery of the hydrophobic drug denbufylline using physically cross-linked palmitoyl glycol chitosan hydrogels. European Journal of Pharmaceutics and Biopharmaceutics, 2003; 55: 35-45.
65. Hervas MJF and Fell JT. Pectin/chotisan mixtures as coating for colon-specific drug delivery: an in vitro evaluation. International Journal of Pharmaceutics, 1998; 169(1): 115-119.
66. Thacharodi D and Panduranga R. Development and invitro evaluation of chitosan-based transdermal drug delivery system for the controlled delivery of propanolol hydrochloride. Biomaterials 1995; 16(2): 145-148.
67. Macleod GS, Collett JH and Fell JT. The potential use of mixed films of pectin, chitosan and HPMC for bimodal drug release. Journal of Controlled Release, 1999; 58(3): 303-310.4\
68. Kawashima Y, Handa T, Kasai A, Takenaka H, Lin SY et al. Novel method for the preparation of controlled-release theophylline granules coated with a polyelectrolyte complex of sodium polyphosphate-chitosan. Indian J.Pharm. Sci, 1985; 74(3): 264-268.
69. Yoshizawa T, Yoshitsune SY, Hong KJ and Kajiuchi Toshio. pH and temperature-sensetive release behaviors from polyelectrolyte complex films composed of chitosan and PAOMA copolymer. Europen Journal of Pharmaceutics and Biopharmaceuticss, 2005; 59: 307-313.

70. Huguet ML, Dellacherie E. Calcium alginate beads coated with chitosan: effect of the structure of encapsulated materials on their release. Process Biochem, 1996; 31(8): 745-751.
71. Sweetman SC (eds.). Martindale – The Complete Drug Reference.28td edn., 1982: 1630.
72. Tripathi KD. Essentials of Medical Pharmacology.Sec.8, Chap. 36-38, 5th edn, 2003; 483: 515-517.
73. Neil IM (eds.). The Merck Index – An Encyclopedia of Chemicals, Drugs & Biologicals. 13th edn. NJ (USA): Merck Research Laboratories, 2001; 3226.
74. Rowe RC, Sheskey PJ, Owen SC. Handbook of Pharmaceutical Excipients.5th edn., 2006; 120-127, 159-161, 656-657.
75. Brazel CS, Peppas NA.Mechanism of solute and drug transport inrelaxing swellable,hydrophilic glassy polymers. Polymers, 1999; 40: 3383-3398.