



FORMULATION DEVELOPMENT AND CHARACTERIZATION OF VORICONAZOLE SUSTAINED RELEASE TABLETS BY USING NATURAL POLYMERS

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ABSTRACT

The objective of the present study was to develop sustained release tablets of voriconazole (350mg) by Natural polymers like chitosan, tamarind gum and fenugreek. The drug excipient mixture were subjected to preformulation studies. The tablets were subjected to physicochemical studies. *In-vitro* drug release kinetic studies. FTIR studies shown there was no interaction between drug and polymer. The physicochemical properties of tablets were found within the limits. The drug release from optimized formulation was for a period of 12 hrs. The kinetic treatment of selected formulation F4 Showed that the release Of drug follows zero order models. results of the present study indicate the suitability of natural polymers in the preparation of sustained release formulation of voriconazole.

Key words: voriconazole, chitosan, tamarind gum, fenugreek and sustained release tablets.

INTRODUCTION

A drug delivery system (DDS) is defined as a formulation or a device that enables the introduction of a therapeutic substance in the body and improves its efficacy and safety by controlling the rate, time, and place of release of drugs in the body¹. This process includes the administration of the therapeutic product, the release of the active ingredients by the product, and the subsequent transport of the active ingredients across the biological membranes to the site of action^{2, 3}. The term therapeutic substance also applies to an agent such as gene therapy that will induce *in vivo* production of the active therapeutic agent. sustained release tablets are commonly taken only once or twice daily, compared with counterpart conventional forms that may have to take three or four times daily to achieve the same therapeutic effect⁴. the advantage of administering a single dose

of a drug that is released over an extended period of time to maintain a near-constant or uniform blood level of a drug often translates into better patient compliance, as well as enhanced clinical efficacy of the drug for its intended use^{5,6}.

The first sustained release tablets were made by Howard press in New Jersey in the early 1950's. The first tablets released under his process patent were called 'Nitroglyn' and made under license by Key Corp in Florida.

Sustained release, prolonged release, modified release, extended release or depot formulations are terms used to identify drug delivery systems that are designed to achieve or extend therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose.

The goal in designing sustained or sustained delivery systems is to reduce the frequency of the dosing or to increase effectiveness of the drug by localization at the site of action, reducing the dose required or providing uniform drug delivery. So, sustained release dosage form is a dosage form that release one or more drugs continuously in predetermined pattern for a fixed period of time, either systemically or to a specified target organ^{7,8}.

Sustained release dosage forms provide a better control of plasma drug levels, less dosage frequency, less side effect, increased efficacy and constant delivery. There are certain considerations for the preparation of extended release formulations:

- ✓ If the active compound has a long half-life, it is sustained on its own,
- ✓ If the pharmacological activity of the active is not directly related to its blood levels,
- ✓ If the absorption of the drug involves an active transport and
- ✓ If the active compound has very short half-life then it would require a large amount of drug to maintain a prolonged effective dose.

The above factors need serious review prior to design.

Introduction of matrix tablet as sustained release (SR) has given a new breakthrough for novel drug delivery system in the field of pharmaceutical technology. It excludes complex production procedures such as coating and pelletization during manufacturing and drug release rate from the dosage form is controlled mainly by the type and proportion of polymer used in the preparations. hydrophilic polymer matrix is widely used for formulating an SR dosage form. Because of increased complication and expense involved in marketing of new drug entities, has focused greater attention on development of sustained release or controlled release drug delivery systems. Matrix systems are widely used for the purpose of sustained release. It is the release system which prolongs and controls the release of the drug that is dissolved or dispersed⁹.

In fact, a matrix is defined as a well-mixed composite of one or more drugs with gelling agent i.e. hydrophilic polymers. by the sustained release method therapeutically effective concentration can be achieved in the systemic circulation over an extended period of time, thus achieving better compliance of patients. Numerous SR oral dosage forms such as membrane controlled system, matrices with water soluble/insoluble polymers or waxes and osmotic systems have been developed, intense research has recently focused on the designation of SR systems for poorly water soluble drugs.

Rationale for extended release dosage forms:

Some drugs are inherently long lasting and require only once-a-day oral dosing to sustain adequate drug blood levels and the desired therapeutic effect. These drugs are formulated in the conventional manner in immediate release dosage forms. However, many other drugs are not inherently long lasting and require multiple daily dosing to achieve the desired therapeutic results. Multiple daily dosing is inconvenient for the patient and can result in missed doses, made up doses, and noncompliance with the regimen^{10,11}. When conventional immediate-release dosage forms are taken on schedule and more than once daily, they cause sequential therapeutic blood level peaks and valleys (troughs) associated with the taking of each dose. However, when doses are not administered on schedule, the resulting peaks and valleys reflect less than optimum drug therapy for example, if doses are administered too frequently, minimum toxic concentrations of drug may be reached, with toxic side effects resulting. If doses are missed, periods of sub therapeutic drug blood levels or those below the minimum effective concentration may result, with no benefit to the patient. Extended-release tablets and capsules are commonly taken only once or twice daily, compared with counterpart conventional forms that may have to be taken three or four times daily to achieve the same therapeutic effect. Typically, extended-release products provide an immediate release of drug that promptly produces the desired therapeutic effect, followed by gradual release of additional amounts of drug to maintain this effect over a predetermined period.

The sustained plasma drug levels provided by extended-release products oftentimes eliminate the need for night dosing, which benefits not only the patient but the caregiver as well.

Advantages of sustained release dosage forms

- The frequency of drug administration is reduced.
- Patient compliance can be improved.
- Drug administration can be made more convenient as well.
- The blood level oscillation characteristic of multiple dosing of conventional dosage forms is reduced.
- Better control of drug absorption can be attained, since the high blood level peaks that may be observed after administration of a dose of a high availability drug can be reduced.
- The characteristic blood level variations due to multiple dosing of conventional dosage forms can be reduced.
- The total amount of drug administered can be reduced, thus:
 - Maximizing availability with minimum dose;
 - Minimize or eliminate local side effects;
 - Minimize or eliminate systemic side effects;
 - Minimize drug accumulation with chronic dosing.
- Safety margins of high potency drugs can be increased as the incidence of both local and systemic adverse side effects can be reduced in sensitive patients.
- Improve efficiency in treatment.
 - Cure or control condition more promptly
 - Improve control of condition

- Improve bioavailability of some drugs
- Make use of special effects; e.g. sustain release aspirin for morning relief of arthritis by dosing before bed-time.

Disadvantages of sustained release dosage forms

- Probability of dose dumping.
- Reduced potential for dose adjustment.
- Cost of single unit higher than conventional dosage forms.
- Increase potential for first pass metabolism.
- Requirement for additional patient education for proper medication.
- Decreased systemic availability in comparison to immediate release conventional dosage forms.
- Poor *invitro* and *invivo* correlations.

MATERIALS AND METHODS

VORICONAZOLE -Procured From Ra Chem Labs, Hyderabad. Provided by SURA LABS, Dilsukhnagar, Hyderabad, Chitosan-Loba Chemie Pvt.Ltd Mumbai, India, Tamarind gum -Merck Specialities Pvt Ltd, Mumbai, India, Fenugreek-Aravind Remedies (AR), Chennai, India, PVP-K 30-Unify chemicals, Jothi Aromas and, DK-Enterprises, India, Aerosil -Merck Specialities Pvt Ltd, Mumbai, India, Magnesium, Stearate-S.D. Fine Chemicals. India, MCC-S.D. Fine Chemicals. India

METHODOLOGY:

Analytical method development:

a) Determination of absorption maxima:

100mg of Voriconazole pure drug was dissolved in 15ml of methanol and make up to 100ml with 0.1N HCL (stock solution-1). 10ml of above solution was taken and make up with 100ml by using 0.1 N HCL (stock solution-2 i.e. 100µg/ml). From this 10ml was taken and make up with 100 ml of 0.1 N HCL (10µg/ml). Scan the 10µg/ml using double beam ultraviolet-visible spectrophotometer in the range of 200 – 400 nm.

b) Preparation calibration curve:

100mg of Voriconazole pure drug was dissolved in 15ml of methanol and volume make up to 100ml with 0.1N HCL (stock solution-1). 10ml of above solution was taken and make up with 100ml by using 0.1 N HCL (stock solution-2 i.e 100µg/ml). From this take 5, 10, 15, 20 and 25 ml of solution and make up to 10ml with 0.1N HCL to obtain 5, 10, 15, 20 and 25µg/ml of Voriconazole per ml of solution. The absorbance of the above dilutions was measured at 255nm by using UV-Spectrophotometer taking 0.1N HCL as blank. Then a graph was plotted by taking Concentration on X-axis and Absorbance on Y-axis which gives a straight line Linearity of standard

curve was assessed from the square of correlation coefficient (R^2) which determined by least-square linear regression analysis. The above procedure was repeated by using pH 6.8 phosphate buffer solutions.

Formulation development of Sustained release Tablets:

All the formulations were prepared by wet granulation method. The compositions of different formulations are given in Table 7.1. The tablets were prepared as per the procedure given below and aim is to prolong the release of Voriconazole.

Procedure:

- 1) Voriconazole and all other ingredients except Magnesium stearate and aerosil were individually passed through sieve no #40.
- 2) Voriconazole, MCC, and polymer mix thoroughly than add the binder solution mix properly up to 15 min.
- 3) Dry the above mixture at 65-70°C by using dryer.
- 4) After completion of drying the mixture is passed through sieve no #22.
- 5) The powder mixture was lubricated with Magnesium stearate and Aerosil.
- 6) Finally go for compression.

Table: Formulation of Sustained release tablets

INGREDIENTS	FORMULATION CHART											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Voriconazole	200	200	200	200	200	200	200	200	200	200	200	200
Chitosan	15	30	45	60	-	-	-	-	-	-	-	-
Tamarind gum	-	-	-	-	15	30	45	60	-	-	-	-
Fenugreek	-	-	-	-	-	-	-	-	15	30	45	60
PVP-K 30	5	5	5	5	5	5	5	5	5	5	5	5
Aerosil	4	4	4	4	4	4	4	4	4	4	4	4
Magnesium Stearate	5	5	5	5	5	5	5	5	5	5	5	5
MCC	121	106	91	76	121	106	91	76	121	106	91	76
Total Weight	350	350	350	350	350	350	350	350	350	350	350	350

Evaluation Parameters

Pre Compression parameters

Bulk density (D_B)

Bulk density is the ratio between a given mass of the powder and its bulk volume.

Bulk density = Mass of Powder / Bulk volume of the powder

Bulk density (D_B) = W / V_{0s}

Procedure: An accurately weighed quantity of granules (w) (which was previously passed through sieve No #40) was carefully transferred into 250 ml measuring cylinder and measure the bulk volume.

Tapped Density (D_T)

Tapped density is the ratio between a given mass of powder (or) granules and the constant (or) fixed volume of powder or granules after tapping.

Tapped density = mass of the powder/ tapped volume

Procedure: An accurately weighed quantity of granules (w) (which was previously passed through sieve No: 40) was carefully transferred into 250 ml measuring cylinder and the cylinder was tapped on a wooden surface from the height of 2.5 cm at two second intervals. The tapping was continued until no further change in volume (until a constant volume) was obtained (V_f). The tapped density was calculated by using the formula

Tapped density (D_T) = W / V_f

Hausner's ratio

Hausner's ratio⁶⁰ is an indirect index of ease of powder flow and was calculated by the formula,

Hausner's ratio = D_T / D_B

Where, D_T is the tapped density

D_B is the bulk density

Compressibility index

Compressibility index (CI) was determined by measuring the initial volume (V_o) and final volume (V_f) after hundred tapping's of a sample in a measuring cylinder. It indicates the powder flow properties and expressed in terms of percentage and given in table no. 14 and calculated by using the formula

% Compressibility index = $(V_o - V_f) / V_o \times 100$

Angle of repose

Angle of repose was measured by fixed funnel method. It determines flow property of the powder. It is defined as maximum angle formed between the surface of the pile of powder and the horizontal plane.

The powder was allowed to flow through the funnel fixed to a stand at definite height (h). By measuring the height and radius of the heap of powder formed (r), angle of repose was calculated by using formula given below and the calculated values obtained was shown in table.

$\theta = \tan^{-1} (h / r)$

Where, θ is the angle of repose

h is the height in cm

r is the radius in cm

Flow property**Table: The flow property of powder blend**

Flow property	Angle of repose	Compressibility index (%)	Hausner's ratio
Excellent	25-30	<10	1.00-1.11
Good	31-35	11-15	1.12-1.18
Fair	36-40	16-20	1.19-1.25
Passable	41-45	21-25	1.26-1.34
Poor	46-55	26-31	1.35-1.45
Very poor	56-65	32-37	1.46-1.59
Very very poor	>66	>38	>1.60

RESULT AND DISCUSSION

The present work was designed to developing sustained release tablets of voriconazole using Natural polymers. All the formulations were evaluated for physicochemical properties and *in vitro* drug release studies.

Analytical Method**Standard graph of Voriconazolein Distil water :**

The scanning of the 10µg/ml solution of Voriconazolein the ultraviolet range (200-400nm) against Distil water the maximum peak observed at λ_{\max} as 255 nm. The standard concentrations of voriconazole(5-25 µg/ml) was prepared in distil water showed good linearity with R² value of 0.998, which suggests that it obeys the Beer-Lamberts law.

Table : Standard curve of Voriconazolein Distil Water

Concentration (µg/ ml)	Absorbance
0	0
5	0.134
10	0.267
15	0.408
20	0.549
25	0.716

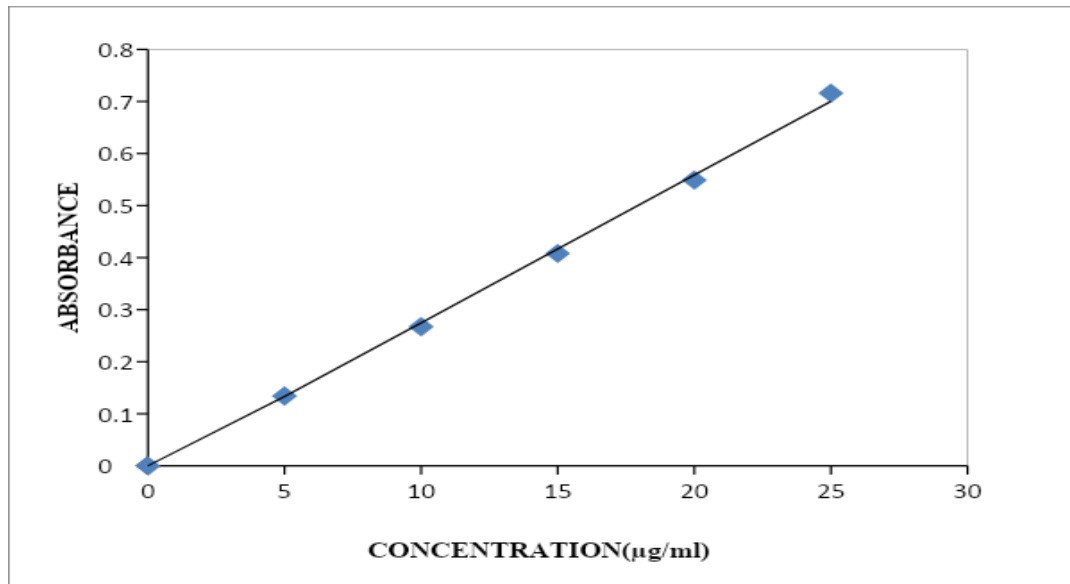


Fig: Calibration curve of Voriconazole in Distilled Water at 255 nm

Standard graph of Voriconazole in 0.1N HCL:

The scanning of the 10 µg/ml solution of Voriconazole in the ultraviolet range (200-400nm) against 0.1 N HCL the maximum peak observed at λ_{\max} as 255 nm. The standard concentrations of Voriconazole (5-25 µg/ml) was prepared in 0.1N HCL showed good linearity with R^2 value of 0.998, which suggests that it obeys the Beer-Lamberts law.

Table: Standard curve of Voriconazole in 0.1N HCL

Concentration (µg/ ml)	Absorbance
0	0
5	0.139
10	0.248
15	0.374
20	0.478
25	0.591

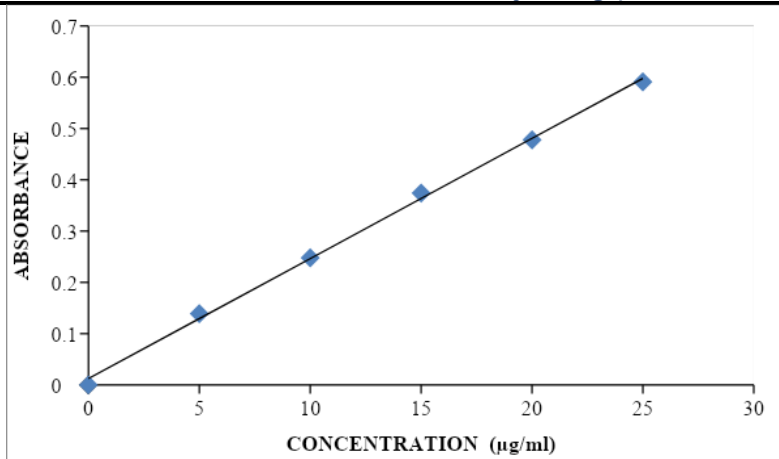


Fig: Calibration curve of Voriconazole in 0.1 N HCL at 255 nm

Standard Curve of Voriconazole in Phosphate buffer pH 6.8

The scanning of the 10 µg/ml solution of Voriconazole in the ultraviolet range (200-400nm) against 6.8 pH phosphate the maximum peak observed at the λ_{max} as 395 nm. The standard concentrations of Voriconazole (5-25 µg/ml) prepared in 6.8 pH phosphate buffer showed good linearity with R^2 value of 0.999, which suggests that it obeys the Beer-Lamberts law

Table: Standard curve of Voriconazole in Phosphate buffer pH 6.8

Concentration (µg / ml)	Absorbance
0	0
5	0.115
10	0.247
15	0.362
20	0.485
25	0.591

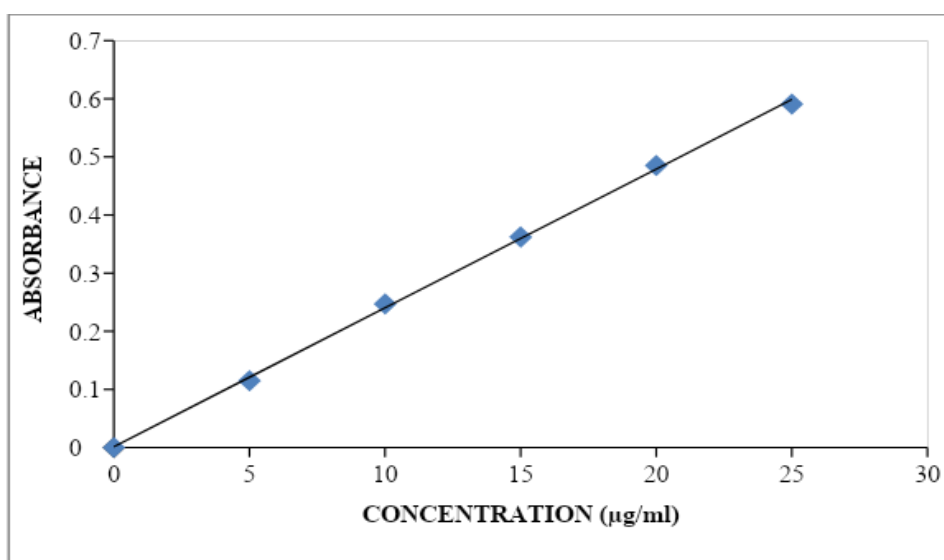


Fig: Calibration of Voriconazole in Phosphate buffer pH 6.8

EVALUATION PARAMETERS**Pre-compression parameters****Table: Pre-compression parameters of powder blend**

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
API	28.13	0.486	0.614	18.12	0.154
F1	18.8	0.38	0.43	11.6	1.13
F2	19.6	0.39	0.44	11.3	1.12
F3	19.4	0.42	0.47	10.6	1.11
F4	21.9	0.40	0.45	11.1	1.12
F5	17.5	0.41	0.46	10.8	1.12
F6	19.2	0.37	0.43	13.9	1.16
F7	19.5	0.38	0.46	17.3	1.21
F8	21.3	0.39	0.45	13.3	1.15
F9	20.1	0.41	0.45	8.8	1.09
F10	19.6	0.41	0.47	12.7	1.14
F11	20.1	0.41	0.46	12.1	1.12
F12	21.5	0.40	0.47	14.89	1.17

Tablet powder blend was subjected to various pre-compression parameters. The angle of repose values was showed from 17.5 to 21.9; it indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.37 to 0.42 (gm/cm³) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.43 to 0.47 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging from 8.8 to 14.89 which showed that the powder has good flow properties. All the formulations were showed the Hausner's ratio ranging from 1.09 to 1.21 indicating the powder has good flow properties.

Post Compression Parameters For Tablets

Table: Post Compression Parameters of Tablets

Formulation codes	Average Weight (mg)	Hardness (kg/cm ²)	Friability (%loss)	Thickness (mm)	Drug content (%)
F1	348.25	5.2	0.24	6.33	98.15
F2	349.62	5.8	0.39	6.25	99.62
F3	350.03	5.6	0.62	6.82	97.68
F4	347.96	5.3	0.48	6.57	99.52
F5	348.58	5.4	0.72	6.35	98.49
F6	349.82	5.7	0.29	6.48	97.19
F7	347.17	5.9	0.48	6.52	99.37
F8	348.79	5.2	0.16	6.61	98.16
F9	349.12	5.6	0.52	6.39	97.31
F10	348.37	5.0	0.49	6.54	99.28
F11	349.62	5.9	0.32	6.72	96.12
F12	349.22	5.7	0.26	6.14	98.42

Weight variation and thickness: All the formulations were evaluated for uniformity of weight using electronic weighing balance and the results are shown in table 8.4. The average tablet weight of all the formulations was found to be between 347.17 to 350.03. The maximum allowed percentage weight variation for tablets weighing >500 mg is 5% and no formulations are not exceeding this limit. Thus all the formulations were found to comply with the standards given in I.P. And thickness of all the formulations was also complying with the standards that were found to be between 6.14 to 6.82.

Hardness and friability: All the formulations were evaluated for their hardness, using Monsanto hardness tester and the results are shown in table 8.4. The average hardness for all the formulations was found to be between (5.0 to 5.9) Kg/cm² which was found to be acceptable.

Friability was determined to estimate the ability of the tablets to withstand the abrasion during packing, handling and transporting. All the formulations were evaluated for their percentage friability using Roche friabilator and the results were shown in table 8.4. The average percentage friability for all the formulations was between 0.16 to 0.72 which was found to be within the limit.

Drug content: All the formulations were evaluated for drug content according to the procedure described in methodology section and the results were shown in table 8.4. The drug content values for all the formulations were found to be in the range of (96.12 to 99.62). According to IP standards the tablets must contain not less than 95% and not more than 105% of the stated amount of the drug. Thus, all the FDT formulations comply with the standards given in IP.

In Vitro Drug Release Studies : The formulations prepared with different polymers by direct compression method. The tablets dissolution study was carried out in paddle dissolution apparatus using 0.1N HCL for 2 hours and 6.8 pH phosphate buffers for remaining hours as a dissolution medium.

Table : Dissolution Data of Voriconazole Tablets Prepared Chitosan in Different Ratios

TIME (hr)	CUMULATIVE PERCENT DRUG RELEASED			
	F1	F2	F3	F4
0	0	0	0	0
1	10.41	13.72	10.58	14.62
2	16.34	18.14	15.64	19.68
3	21.92	25.76	27.11	25.64
4	28.76	35.10	38.97	31.48
5	33.63	46.28	45.65	36.95
6	45.21	55.19	52.74	48.72
7	49.34	64.98	64.22	59.39
8	57.27	69.75	75.94	63.14
9	68.34	74.15	84.19	67.58
10	73.27	79.37	88.76	74.11
11	81.54	85.48	92.36	80.64
12	87.12	91.86	95.15	98.96

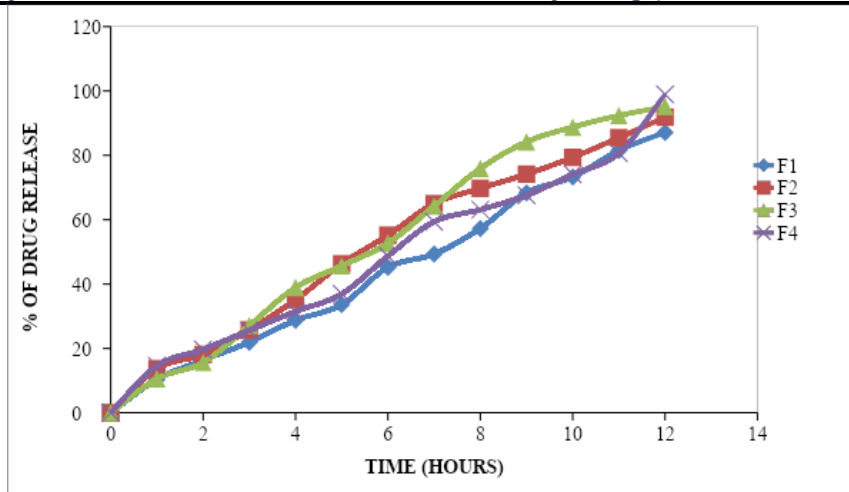


Figure : Dissolution study of Voriconazole Sustained tablets (F1 to F4)

Table : Dissolution Data of Voriconazole Tablets Prepared With Tamarind gum in Different Concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG RELEASED			
	F5	F6	F7	F8
0	0	0	0	0
1	12.52	8.39	7.19	10.96
2	17.37	16.17	19.72	14.83
3	27.48	25.35	23.93	21.78
4	42.26	36.17	29.54	27.41
5	54.18	48.86	35.41	35.79
6	58.71	56.61	39.76	41.86
7	66.33	69.14	56.19	47.31
8	75.85	75.59	64.72	53.22
9	83.95	83.61	67.29	61.89
10	86.78	85.34	72.34	67.15
11	90.15	89.23	76.52	72.93
12	96.15	92.45	84.42	76.42

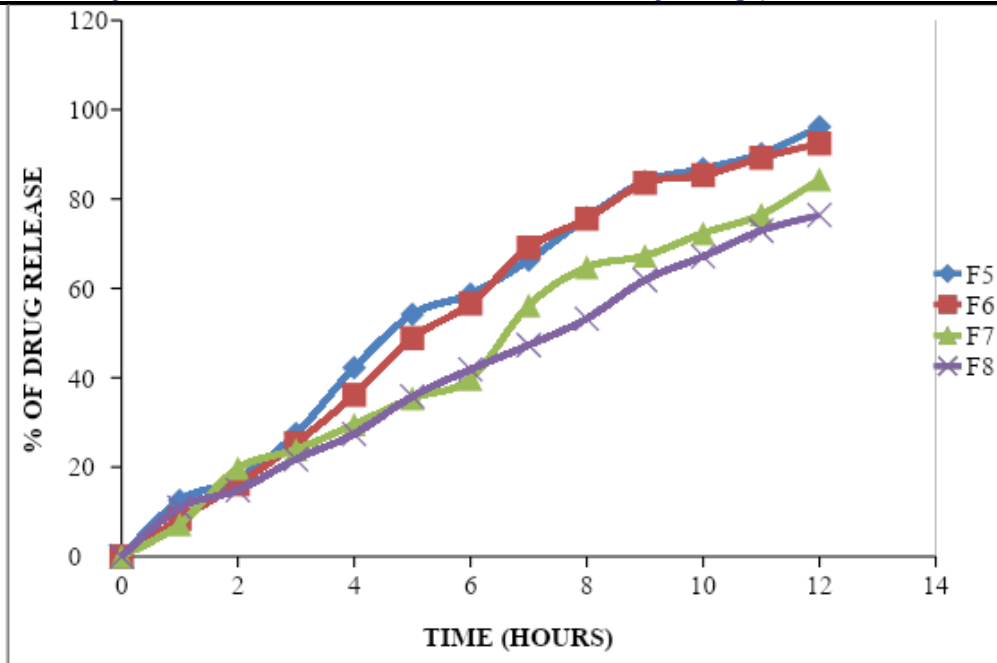


Figure : Dissolution study of Voriconazole tablets (F5 to F8)

Table : Dissolution Data of Voriconazole by using Fenugreek

TIME (hr)	CUMULATIVE PERCENT DRUG RELEASED			
	F9	F10	F11	F12
0	0	0	0	0
1	12.38	8.36	9.39	6.35
2	18.29	14.49	19.75	13.92
3	23.71	26.38	26.31	18.72
4	32.92	34.97	32.68	28.92
5	38.49	48.11	48.97	34.89
6	46.58	53.38	57.45	47.22
7	58.26	65.15	65.53	53.81
8	69.15	74.59	72.97	59.78
9	76.87	78.67	75.32	63.75
10	84.62	82.98	82.47	69.18
11	88.48	87.35	85.59	73.82
12	94.12	90.24	87.67	78.49

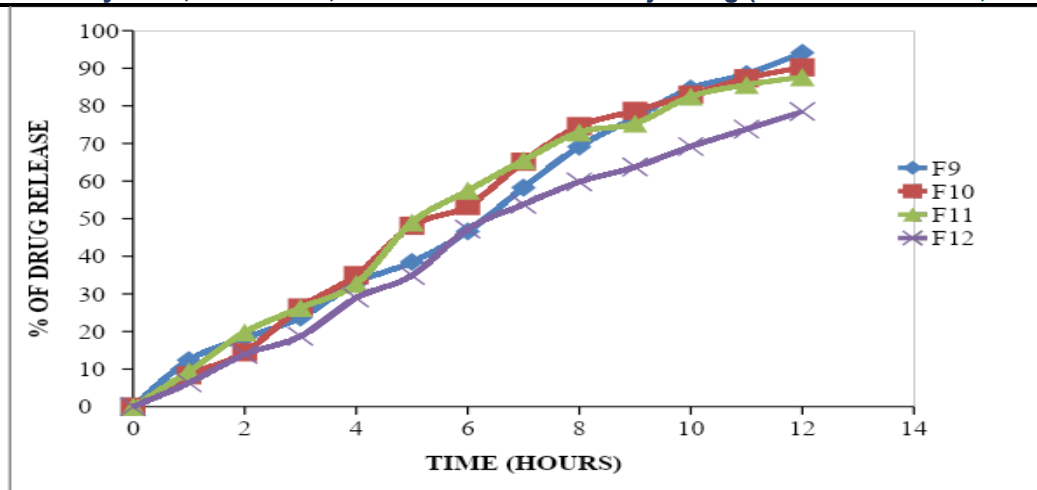


Figure: Dissolution study of Voriconazole tablets (F9 to F12)

From the tabular column 8.5 it was evident that the formulations prepared with Chitosan as retarding polymer in low concentrations the polymer was unable to produce the required retarding action to the tablets. As the concentration of polymer increases the retarding nature was also increased. Chitosan in the concentration of 60 mg showed good % drug release i.e., 98.96 in 12 hours.

Where as in case of formulations prepared with Tamarind gum as retarding polymer, the formulations with 15 mg concentration of polymer showed complete drug release in 12 hours only, whereas the concentration of polymer increases the retarding nature decreased. The Formulation Containing Tamarind gum in 15 Mg Concentration Showed good retarding nature with required drug release in 12 hours i.e., 96.15 %.

Where as in case of formulations prepared with Fenugreek as retarding polymer, the formulations with 15 mg concentration of polymer showed complete drug release in 12 hours only, The Formulation Containing Fenugreek in 15 Mg Concentration Showed good retarding nature with required drug release in 12 hours i.e., 94.12 %.

From the above results it was evident that the formulation F4 is best formulation with desired drug release pattern extended up to 12 hours.

Application of Release Rate Kinetics to Dissolution Data

Data of *in vitro* release studies of formulations which were showing better drug release were fit into different equations to explain the release kinetics of Voriconazole release from Sustained tablets. The data was fitted into various kinetic models such as zero, first order kinetics; Higuchi and Korsmeyer Peppas mechanisms and the results were shown in below table

Table : Release kinetics data for optimized formulation (F4)

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG (%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM % RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Q11/3	Q01/3-Q11/3
0	0	0			2				100	4.642	4.642	0
14.62	1	1	1.165	0	1.931	14.62	0.0684	-0.835	85.38	4.642	4.403	0.238
19.68	2	1.414	1.294	0.301	1.905	9.84	0.0508	-0.706	80.32	4.642	4.315	0.327
25.64	3	1.732	1.409	0.477	1.871	8.547	0.039	-0.591	74.36	4.642	4.205	0.436
31.48	4	2	1.498	0.602	1.836	7.87	0.0318	-0.502	68.52	4.642	4.092	0.55
36.95	5	2.236	1.568	0.699	1.8	7.39	0.0271	-0.432	63.05	4.642	3.98	0.661
48.72	6	2.449	1.688	0.778	1.71	8.12	0.0205	-0.312	51.28	4.642	3.715	0.926
59.39	7	2.646	1.774	0.845	1.609	8.484	0.0168	-0.226	40.61	4.642	3.437	1.204
63.14	8	2.828	1.8	0.903	1.567	7.893	0.0158	-0.2	36.86	4.642	3.328	1.314
67.58	9	3	1.83	0.954	1.511	7.509	0.0148	-0.17	32.42	4.642	3.189	1.453
74.11	10	3.162	1.87	1	1.413	7.411	0.0135	-0.13	25.89	4.642	2.958	1.683
80.64	11	3.317	1.907	1.041	1.287	7.331	0.0124	-0.098	19.36	4.642	2.685	1.956
98.96	12	3.464	1.995	1.079	0.017	8.247	0.0101	-0.005	1.04	4.642	1.013	3.628

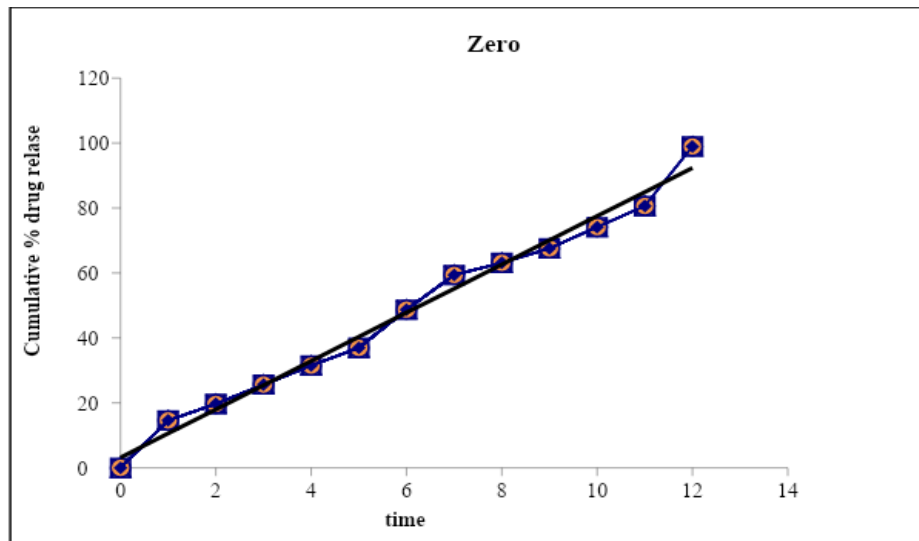


Figure : Graph of zero order kinetics

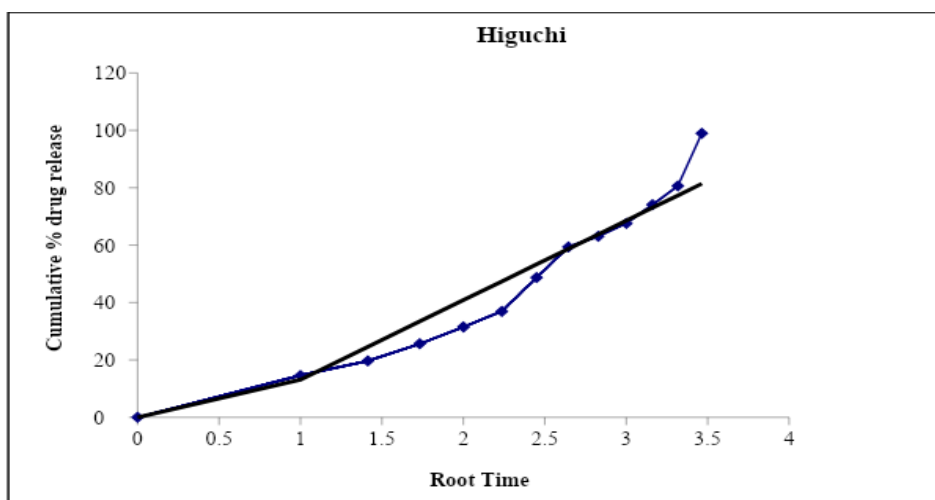


Figure: Graph of higuchi release kinetics

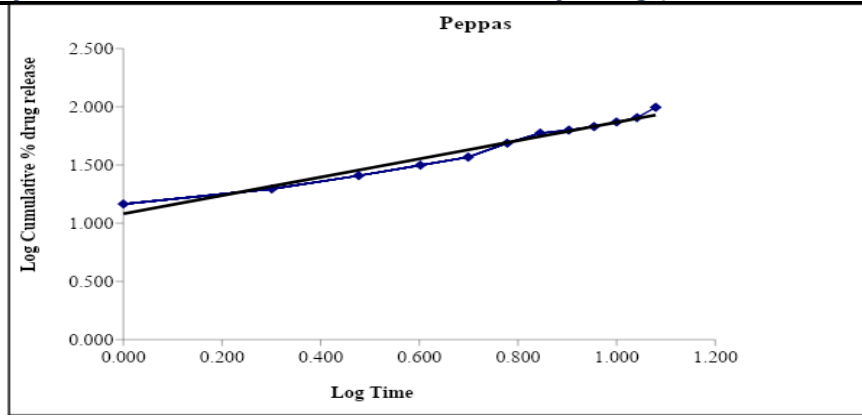


Figure: Graph of peppas release kinetics

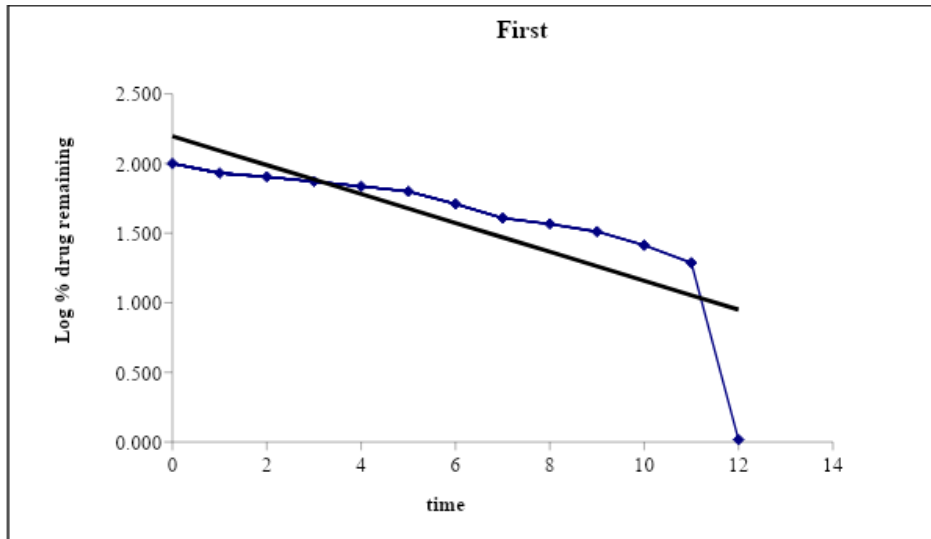


Figure: Graph Of First Order Release Kinetics

Based on the data above results the optimized formulation followed zero order kinetics.

Drug and Excipient Compatibility Studies

FTIR STUDY

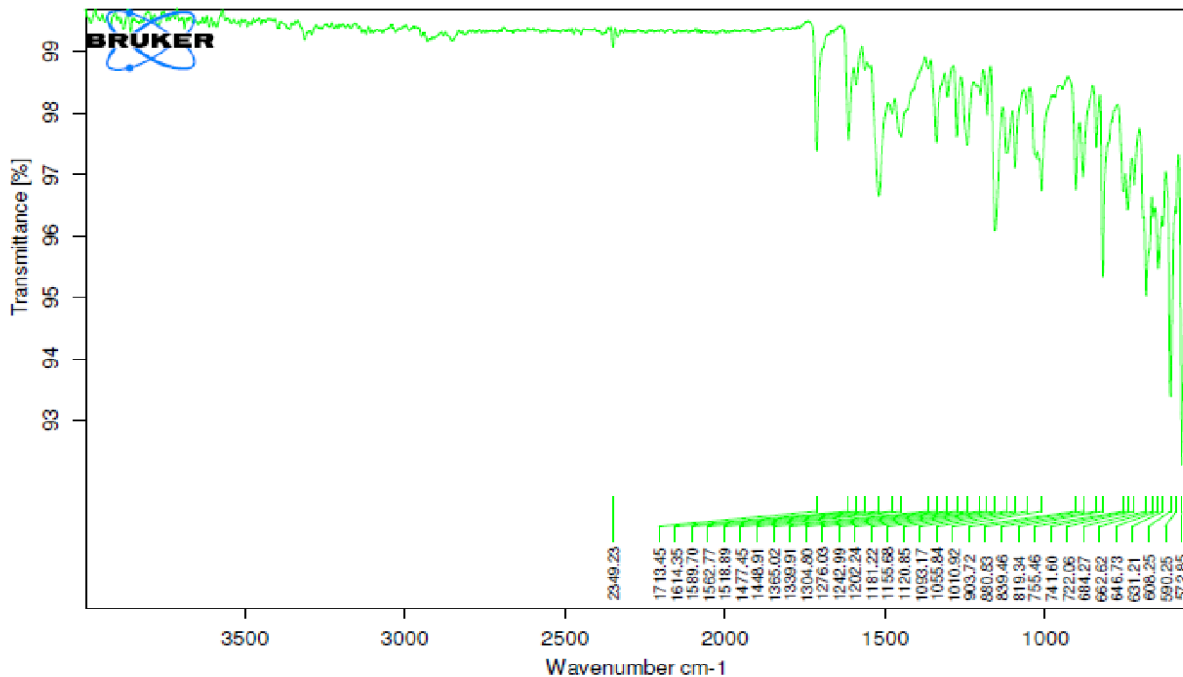


Fig: FT-IR graph Of pure Drug

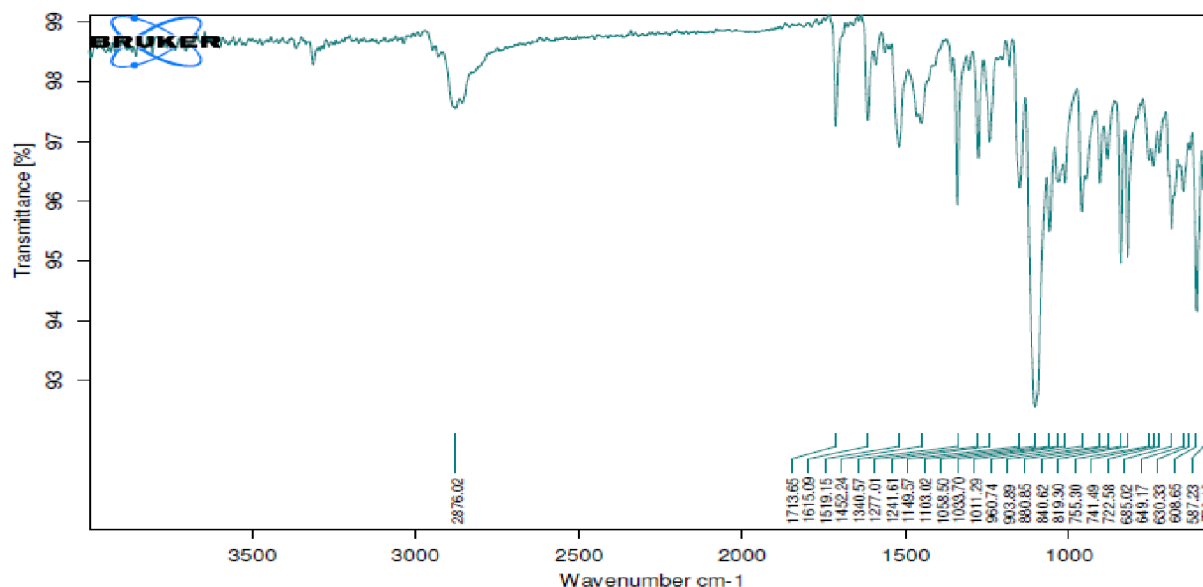


Fig: FT-IR graph Of optimised formulation

From the FT-IR data it was evident that the drug and excipients doses not have any interactions. Hence they were compatible.

CONCLUSION

The sustained release tablets of Voriconazole were prepared by wet granulation method. FTIR spectra indicated the absence of probable chemical interaction between the drug and polymers. Voriconazole sustained release matrix tablets were formulated with different polymers like chitosan, tamarind gum and fenugreek (azithromycin chitosan) is optimized. Among 12 formulations F4 is optimized based on the % drug release is 98.96 in 12 hrs. The *in vitro* drug release data was plotted for various kinetic models. The R^2 value for optimized formulation F4 for zero order was found to be 0.986.

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