FORMULATION AND EVALUATION OF MATRIX TABLETS OF ROPINIROLE HYDROCHLORIDE FOR ORAL CONTROLLED RELEASE

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ABSTRACT

The objective of the present investigation is to prepare and evaluate the controlled release matrix tablets of a water soluble drug (ropinirole hydrochloride) using direct compression and Wet granulation technology. Ropinirole Hydrochloride is a hydrophilic drug and has pH independent solubility. It is used in the treatment of idiopathic parkinsonsdisease. The controlled release matrix tablets of ropinirole hydrochloride were prepared using various polymers: guargum, sodium alginate and carbopol 940P.The matrix tablets were prepared using two strategies: direct compression and wet granulation. The tablets were evaluated for the various quality control parameters and the drug release was evaluated in pH 1.2 and in pH 7.4 buffer. The optimized formulation containing drug and guar gum controlled the drug release up to 8 hours. The drug release from the optimized formulation (drug: guar gum,1:2.5) followed first order kinetics and showed non-fickian diffusion mechanism. The FTIR studies indicated the lack of drug-polymer interaction. The formulated controlled release tablets can decrease the frequency of drug administration, decrease the plasma drug fluctuation and it can improve the patient compliance.

Key words*: Ropinirole Hydrochloride, Controlled release, matrix tablets*

INTRODUCTION

The oral route of drug delivery is one of the most convenient means to administer drug to the human body to obtain the desired therapeutic effect. Though it is a convenient route it provides several challenges to the formulator to design a medication such that it provides the drug in an optimum concentration needed to attain a plasma level of the drug which will fall within the therapeutic window to obtain the desired effect. Conventional dosage forms are unable to control either the rate of delivery or target the desired site of delivery. As a result, there is a large redistribution of the drug to the non-target tissues which exceeds the amount needed for the therapeutic activity which often leads to serious adverse effects in the treatment. Conventional dosage forms are rapidly absorbed with “peak” and “valley” or “saw tooth” kinetic plasma concentration profiles. Controlled delivery systems have been introduced to overcome all these above stated disadvantages of the conventional release systems.

All controlled release products share the common goal of improving drug therapy over that achieved with their non-controlled counter parts. This improvement in drug therapy is represented by several potential advantages of the controlled release systems: decreased local and systemic side effects, reduced gastrointestinal irritation, better drug utilization, more uniform blood concentration, reduction in fluctuation in drug level and hence more uniform pharmacological response. For drugs with very short elimination half-lives, controlled release products maintain the efficacy over a long duration and improve the patient compliance’. With many drugs, the basic goal of therapy is to achieve a steady state blood or tissue level which is therapeutically effective and nontoxic for an extended period of time. Conceptually, an ideal drug delivery system should fulfill two prerequisites: the first is to deliver the drug at a rate dictated by the needs of the body over the period of treatment, and the second is spatial targeting to specific site(s)[1]. Furthermore, the possibility of re-patenting successful drugs, coupled with the increasing expense in bringing new drug entities to market, has been instrumental in generating interest in controlled-release drug delivery systems (CRDDS).

Controlled-release[2] dosage forms are gaining rapid popularity in clinical medicine. The more sophisticated systems are used to alter the pharmacokinetic behavior of drugs in order to provide twice- or once-a-day dosage. Controlled release drug delivery systems are designed by different techniques like enteric coating, osmotic pump, prodrugs, transdermal patches and matrix tablets[3,4]. Among the various techniques used in the recent times, the pharmaceutical researchers have been attracted by the matrix tablets because of their ease of manufacturing[5,6]. Different types of polymers[7,8] are used to control the release of drugs from the dosage forms for absorption by the human body. Though a variety of polymeric substances are available to serve as release retarding matrix materials there is a continued need to develop new, safe and effective release retarding materials for matrix tablets[9]. Natural gums and polysaccharides and their derivatives represent a group of polymers widely used in pharmaceutical dosage forms due to their non-toxicity, low cost and free availability. Natural gums and hydrophilic polymers when in contact with water, they are hydrated to form a gel. Because of this property polymers like guar gum gum, xanthan gum and HPMC have been reported as good matrix materials[10,11] in controlled release dosage forms.

Ropinirole[12-14]is a non-ergoline dopamine agonist with high relative *in vitro* specificity and full intrinsic activity at the D2 and D3 dopamine receptor subtypes, binding with higher affinity to D3 than to D2 or D4 receptor subtypes. It acts by the stimulation of postsynaptic dopamine D2-type receptors with in the caudate-putamen in the brain. Ropinirole is indicated for the treatment of the signs and symptoms of idiopathic parkinson'sdisease. It is a water soluble (133 mg/ml,it has pH independent solubility)potent drug and is available in different strengths (0.25 mg, 0.5 mg, 1 mg, 2 mg, 4 mg or 5 mg) of tablets. RopiniroleHCl has short elimination half-life (3-4 hours) and is adminstered 3-4 times a day.The aim of the present investigation was to formulate controlled release tablets of ropiniroleHCl to reduce the frequency of administration, prolong its duration of action and to improve the patient compliance.

MATERIALS AND METHODS

RopiniroleHCl was obtained as a gift sample from Dr. Reddys Labs., Hyderabad. Guar gum, sodium alginate, Carbopol 940P and microcrystalline cellulose were procured from S.D Fine Chem. Ltd., Mumbai.

Preformulation studies were conducted to estimate the angle of repose, bulk density, compressibility index and hausner's ratio. Melting point of the pure drug was estimated by using the melting point apparatus (Campbell).The melting point of the pure drug was found to be 246^{o}C. The partition coefficient of the drug was estimated using the n-octanol and water as the immiscible solvents. The value of the partition coefficient was found to be, Log P(n-Octanol/water)=2.7.The pH of the aqueous drug solution was estimated using the pH meter(Elico). The pH of the aqueous drug solution was 6.4 .Formulation development studies were carried out using two different strategies: wet granulation technique and direct compression technique.

EVALUATION OF POWDER BLEND

The drug-excipient blend used for preparing the different tablet formulations was evaluated for the following parameters:

Angle of Repose: Angle of repose*is* defined as the maximum angle possible between the freely sliding surface of the pile of the powder and the horizontal plane. Angle of repose of different formulations was measured according to fixed height funnel standing method,

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

Where, h = height of pile, r = radius of the base of the pile,θ = angle of repose

Bulk Density and Tapped Density: Bulk density and tapped density were measured by using 10 ml graduated cylinder. The sample poured in the cylinder was tapped mechanically for 100 times, and then the tapped volume was noted down. Bulk density and tapped density were calculated. Each experiment for micrometric properties was performed in triplicate. Bulk Density = (Weight of the powder blend/ Bulk volume).Tapped Density = (Weight of the powder blend / Tapped volume).

Carr's Index: Carr's index value of the powder blend was computed according to the following equation: Carr index(%) = [(Tapped density – Bulk Density) / Tapped Density] × 100

Hausner's Ratio: Hausner's ratio of the drug-excipient powder blend was determined by comparing the tapped density to the bulk density using the equation: Hausner's Ratio = Tapped density / Bulk Density.

ESTIMATION OF ROPINIROLEHCL

RopiniroleHCl was estimated by the U.V. spectrophotometric method. The calibration curve was constructed in both pH1.2 and pH 7.4 phosphate buffer by using the U.V. spectrophotometer (Analytical). In pH 1.2, the Beer lamberts concentration range was 2 to 20 µg/ml. In pH 7.4 buffer, the Beer lamberts concentration range was 2 to 30 µg/ml .The value of slope and intercept in pH 1.2 was 0.0304 and 0.0029 respectively. The value of slope and intercept in pH 7.4 buffer was 0.0284 and 0.0012 respectively. In both pH 1.2 and pH 7.4 buffer, the absorption maxima was obtained at 250 nm[15].

Formulation Development: Two strategies have been adopted to extend the release of freely water soluble drug from the formulation they are: Wet granulation technique and direct compression technique.

WET GRANULATION TECHNIQUE

The composition of the formulations is given in table 1 and the Extended Release Matrix tablets of Ropinirole Hydrochloride were formulated using wet granulationmethod. The 5% polyvinyl pyrrolidone in ethanol was used as the binder solution. Binder solution was added to the drug-excipient blend and it was mixed.The wet mass was passed through # 10 .The wet granules were dried in the tray dryer (at 60°C) for 1 hour. The dried granules were passed through #20.Talc and magnesium stearate, which are previously passed through #80, was added to the dried granules and it was mixed, the blend was compressed in to tablets. The 50 tablets were prepared in each batch. While granulation is done using sieve number10, for regranulation sieve number 20 is used. Initially we used sieve no. 10 for granulation of wet mass. After drying, the granules were passed through sieve no. 20.The same procedure has been reported for the preparation of Phenobarbitone tablets[16].

Table-1: Composition of tablets prepared by strategy I

INGREDIENTS(mg)	F1	F2	F3	F4	F5	F6
RopiniroleHCl	2	2	2	2	2	2
Guar Gum	-	-	-	1	2	5
Sodium Alginate	1	2	5	-	-	-
Magnesium Stearate	3	3	3	3	3	3
Talc	3	3	3	3	3	3
Micro Crysalline Cellulose	291	290	287	291	290	287

Direct Compression Technique:

The composition of the formulations are given in the table 2 and the Extended Release Matrix tablets of Ropinirole Hydrochloride were formulated using direct compressionmethod. All the ingredients were sieved i.e., drug, filler and the rate controlling polymers are passed through #30 sieve. This blend was then lubricated with magnesium stearate (previously passed through #80), mixed properly in a polybag. The prepared blend was compressed using single stage tablet compression machine. The 50 tablets were prepared in each batch.

Table 2: **Composition of tablets prepared by stategy II**

INGREDIENTS(mg)	F7	F8	F9	F10	F11	F12	F13	F14
RopiniroleHCl	2	2	2	2	2	2	2	2
Guar gum	5	-	-	2	-	-	-	1
SodiumAlginate	-	5	-	-	2	-	1	-
Cabopol 940P	-	-	5	-	-	2	-	-
Magnesium Stearate	3	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3	3
Micro crystalline cellulose	287	287	287	290	290	290	291	291

EVALUATION OF TABLETS

The formulated tablets were evaluated for the following physicochemical characteristics:

Hardness: Hardness of the tablet was determined by using the Monsanto hardness tester. The lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by turning a threaded bolt until the tablet fractured. As the spring was compressed a pointer rides along a gauge in the barrel to indicate the force required for the tabletto break.

Weight Variation: The 20 tablets were selected and weighed collectively and individually. From the collective weight, average weight was calculated. Each tablet weight was then compared with average weight to ascertain whether it was within the permissible limits or not. Not more than two of the individual weights deviated from the average weight by more than 7.5% for 300 mg tablets and none by more than double that percentage.

Friability test: The 20 previously weighed tablets were placed in the friability apparatus, which was given 100 revolutions and the tablets were reweighed. The percentage friability was calculated by using the following formula,

Percentage friability = initial weight-final weight /initial weight × 100.

DISSOLUTION STUDIES

Dissolution studies were conducted by taking 900 ml of 0.1N HCl as the dissolution media for the first two hours period and replacing the medium with 900 ml of pH 7.4 phosphate buffer for the next six hours. USP Dissolution Apparatus II (paddle) was used at 37^{o} Cand100 rpm... Samples for dissolution study were withdrawn at 1/2hr, 1hr, 2hr, 3hr, 4hr, 6hr, and 8hr. At these time intervals the samples (5 ml) of the solution was withdrawn from the dissolution apparatus and the samples were replaced with fresh dissolution medium to maintain the sink condition. Samples which were collected as a part of the dissolution study were analyzed by UV-VISIBLE Spectrophotometer (Analytical).

Assay: The twenty tablets of ropinirole hydrochloride were weighed and powdered in glass mortar. Powder equivalent to 10 mg of the drug was transferred to 100 ml volumetric flask, dissolved in about 50 ml distilled water and the volume was adjusted to the mark with distilled water. The absorbance of solutions was measured at 250 nm. The concentration of ropinirole hydrochloride was determined by refering to the calibration curve.

RELEASE KINETICS

The analysis of drug release mechanism from a pharmaceutical dosage form is an important but complicated process and is practically evident in the case of matrix systems. As a model-dependent approach, the dissolution data was fitted to four popular release models such as zero-order, first-order, diffusion and Peppa's-Korsemeyer equations. The order of drug release from the matrix systems was described by using zero order kinetics or first orders kinetics. The mechanism of drug release from the matrix systems was studied by using Higuchi equation and Peppa's-Korsemeyer equation.

Zero Order Release Kinetics: It defines a linear relationship between the fractions of drug released versus time. $Q = k_o t$. Where, Q

is the fraction of drug released at time t and $k_o$is the zero order release rate constant. A plot of the fraction of drug released against time will be linear if the release obeys zero order release kinetics.

First Order Release Kinetics: Wagner assuming that the exposed surface area of a tablet decreased exponentially with time during dissolution process suggested that drug release from most of the slow release tablets could be described adequately by apparent first-order kinetics. The equation that describes first order kinetics is in (1-Q) = - K_1t.Where, Q is the fraction of drug released at time t and k_1 is the first order release rate constant. Thus, a plot of the logarithm of the fraction of drug undissolved against time will be linear if the release obeys first order release kinetics.

Higuchi Equation: It defines a linear dependence of the active fraction released per unit of surface (Q) on the square root of time. $Q=K_2t^{½}$ .Where, K2 is the release rate constant. A plot of the fraction of drug released against square root of time will be linear if the release obeys Higuchi equation[17].

Power Law: In order to define a model, which would represent a better fit for the formulation, dissolution data was further analyzed by Peppa's and Korsemeyer equation (Power Law). $M_t/M_\alpha = K.t^n$.Where, M_t is the amount of drug released at time t and M_α is the amount released at time α, thus the $M_t/M_\alpha$is the fraction of drug released at time t, k is the kinetic constant and n is the diffusion exponent. A plot between log of M_t/M_α against log of time will be linear if the release obeys Peppa's and Korsemeyer equation and the slope of this plot represents "n" value[18].

FOURIER TRANSFORM INFRARED SPECTROSCOPY (FTIR) STUDIES

FTIR spectra of the drug (ropiniroleHCl), sodiumalginate, guar gum, physical mixture of drug and sodium alginate, physical mixture of drug and guar gum were studied to confirm the compatibility of the drug with the polymer. FTIR spectroscopy was obtained by a FTIR spectrophotometer (Bruker) using KBr pellets and the scanning range used was 4400 to 400 cm^{-1} at a scan period of 1min.

RESULTS AND DISCUSSION

Extended release tablets have come into light due to the development of several new chemical entities which have high solubility and short elimination half-life. Rate controlling polymers are employed to decrease the dissolution rate and to extend the release of the water soluble drug.

Preparation of tablets: In one strategy (I), matrix formers: Guar gum and Sodium alginate were used in different quantities by using Wet Granulationmethod. In the second strategy(II),the matrix fomers: guargum, sodium alginate and Carbopol 940 P were employed in different quantities and formulated by using Direct Compression technique. RopiniroleHCl has solubility independent of pH, i.e it is freely soluble in all pHvalues. Standard curve of RopiniroleHClwas constructed in pH 7.4 phosphate buffer and in 0.1N HCl, by plotting absorbance against concentration at 250 nm, and it follows the Beer's lambert law. Extended Release tablets of Ropinirole hydrochloride were prepared. In the present study 14 formulations with variable concentration of polymers were prepared and evaluated for physico-chemical parameters and the *in vitro* release .The formulated batches are shown in table no:1and 2.The angle of repose for the drug-excipient blend was carried out and it was found to range from 20°.88'to 29°.88'and the results are shown in table 3and 4.The bulk density for the drug-excipient blend, ranged between 0.404-0.60 g/ml , the results were shown in table 3 and 4.The tapped density of the drug-excipient blend for the different batches ranged from 0.603-0.77g/ml. Compressibility index of the drug-excipient blend was carried out, it was found range between 16.26% to 34.72% ,the results are shown in table 3and 4.The values of Hausner ratio of the drug-excipient blend for the different batches ranged from 1.19-1.53.

Table 3: Pre-compression Parameters of drug-excipient blend for strategy I

Powder blend	Angle of Repose (Ø)	Bulk Density (g/ml)	Tapped Density (g/ml)	Compressibility Index (%)	Hausner ratio
F1	24°	0.59	0.77	23.41	1.33
F2	23°.5'	0.6	0.765	19.91	1.27
F3	22°	0.562	0.692	18.78	1.23
F4	20°.8'	0.551	0.656	16.26	1.19
F5	21°.9'	0.556	0.684	18.71	1.22
F6	22°.5'	0.557	0.679	17.96	1.21

Table 4: Pre-compression Parameters of drug-excipient blend for strategy II

Powder blend	Angle of Repose (Ø)	Bulk Density (g/ml)	Tapped Density (g/ml)	Compressibility Index (%)	Hausner ratio
F7	24°.30'	0.422	0.600	29.57	1.42
F8	26°.77'	0.461	0.666	29.41	1.5
F9	25°.28'	0.410	0.652	34.24	1.52
F10	28°.56'	0.447	0.638	29.85	1.42
F11	29°.88'	0.434	0.652	33.33	1.41
F12	25°.30'	0.416	0.638	34.72	1.53
F13	26°.47'	0.404	0.603	32.432	1.48
F14	24°.28'	0.428	0.612	30.00	1.42

Evaluation of tablets: The different tablet formulations were physically characterized by parameters like thickness, average weight, hardness, friability, uniformity of weight, and in *vitro* dissolution studies. All the formulated tablets complied with the official pharmacoepial limits of weight variation, hardness, friability and the assay values. The thickness of the formulations was found in the range of 5.5-5.7mm. The tablets exhibited uniform thickness among the different formulations (table 5 and 6).The hardness of the tablets of all the batches ranged between 6 to 8 kg/cm^2 which was sufficient to maintain the mechanical strength. The results of hardness tests are given in table 5 and 6.The percentage friability of the formulated tablets ranged from 0.13-0.48%. In the present study, the percentage friability for all the formulations was found to be below 0.48% indicating that friability (%) is within the acceptable limits. The results of friability test are depicted intable 5 and 6.The percentage deviation for the average weight of all tablet formulations was found within ± 5% and hence all the formulations pass the test for uniformity of weight. Good uniformity in drug content was found amongst the different batches of the tablets, the percentage drug content of the formulated tablets was found to be in the range, 98.01%-103.9%.

Table 5: Post -Compression parameters of tablets for strategy I

Formulations	Average Weight(mg)±S.D. (n = 20)	Friability (%) (n = 10)	Hardness (kg/cm^2) (n = 3)	Thickness (mm) (n = 5)	Assay (%) (n = 6)
F1	298±0.6	0.21	7-8	5.6	98.02
F2	289±0.9	0.13	7-8	5.7	103.9
F3	305±0.8	0.24	7-8	5.6	99.53
F4	305±0.7	0..16	6-8	5.5	98.01
F5	298±0.6	0.21	6-8	5.6	101.1
F6	295±0.8	0.19	6-8	5.6	99.3

Table 6: Post -Compression parameters of tablets for strategy II

Formulations	Average Weight (mg)±S.D. (n = 20)	Friability (%) (n = 10)	Hardness (kg/cm²) (n = 3)	Thickness (mm) (n =5)	Assay (%) (n = 3)
F7	298±0.9	0.32	7-8	5.7	102.3
F8	300±0.7	0.36	7-8	5.6	101.2
F9	305±0.9	0.42	6-8	5.6	99.3
F10	289±0.8	0.48	6-8	5.7	103.9
F11	303.5±0.6	0.44	7-8	5.6	99.53
F12	310±0.8	0.48	6-7	5.5	98.01
F13	300±0.7	0.41	7-8	5.6	101.1
F14	305±0.8	0.47	7-8	5.6	99.3

Dissolution Studies: Dissolution studies were carried out in 0.1N HCl as the dissolution media for the first two hours period and replacing the medium with pH 7.4 phosphate buffer for the next six hours (fig.1-5).From the above drug release data, the results indicated that the formulation containing drug: guar gum in the ratio of 1:2.5 (batch F7) had shown the optimum release. It was observed that by increasing the amount of polymer in the matrix, the matrix showed a progressive decrease in the drug release. An increase in the amount of the polymer in the matrix tablets leads to a slower release rate. Hence, a balance between the amounts of the polymer components was necessary to obtain the desired release profile. In the present study, sodiumalginate, guar gum and Carbopol 940 P were used as the hydrophilic matrix polymers, because these polymers form a strong viscous gel on contact with the aqueous media, which may be useful in the controlled delivery of highly water-soluble drugs. In an attempt to extend the release of the drug, the concentration of guar gum, sodium alginate and Carbopol 940P were increased. Faster release of the drug from the matrix tablets(when low concentration of polymers were used) was probably due to faster dissolution of the highly water-soluble drug from the core and its diffusion out of the matrix, forming the pores for the entry of the solvent molecules. When the polymer concentration was increased in the tablets, the drug release was decreased, possibly due to the reduction in the penetration of the solvent molecules into the system because of the viscous nature of the formulation (when higher concentration of the polymer was used).

In vitro drug release studies revealed that the release of ropiniroleHCl from the different formulations varies with the characteristics and the composition of the matrix forming polymers as shown in Fig.1-5.The release rate of the drug decreased with increasing concentration of the polymers(sodium alginate, guar gum and Carbopol 940P).These findings are in compliance with the ability of the hydrophilic polymers to form complex matrix network which leads to delay in the release of the drug from the device. In the present investigation, as the polymer concentration was increased, the drug release was decreased; because the polymers formed a viscous gel and there was a reduction in the rate of drug release. In the wet granulation technique, when sodium alginate was used as the polymer, the drug release was found to be in the order:F1(drug:sodium alginate,1:1)>F2(drug:sodium alginate,1:2)>F3(drug:sodium alginate,1:3).Similarly,when guar gum was used as the polymer(wet granulation),the drug release followed the order:F4(drug:guar gum,1:1)>F5(drug:guar gum,1:2)>F6(drug:guar gum,1:3).In the direct compression technique,the drug release followed the order:F14(drug:guar gum,1:1)>F10(drug:guargum,1:2)>F7(drug: guar gum,1:5).Similarly,for the sodium alginate containing tablets,the drug release exhibited the oder F13(drug:sodiumalginate, 1:1)>F11(drug:sodiumalginate, 1:2)>F8(drug:sodium alginate,1:5).For the carbopol containing tablets,the drug release followed the order F12(drug:carbopol,1:2)>F9(drug:carbopol,1:5).When matrices containing swellable polymers are exposed to dissolution

medium, tablet surface becomes wet and hydrated to form a gel layer. The initial release of drug from these matrices occurs by the drug dissolution in the water penetrated in to the matrix. The overall drug release from these matrices is governed by hydration, gel layer formation and drug diffusion in to the gel layer and to the dissolution media. Polymer erosion also plays a major role in releasing drug from these matrices. These considerations indicate that hydrophilic polymers have the potential to control the release of drug from the matrix tablets. The release of drug is regarded as concentration of polymer increases in all the formulations. When low concentration of polymer was used the faster drug release might be due to rapid swelling and surface erosion of the matrix. Also, the viscous gel layer is not formed around the tablet when low concentration of polymer is used, hence it allows rapid diffusion of drug in uncontrollable manner which is insignificant to retard the drug release for prolonged period of time. When high concentration of polymer is used, a viscous gel layer is formed around the tablet, resisting erosion and the diffusion of the drug is controlled primarily by the gel viscosity. The viscosity of polymer solutions strongly increases with increasing concentration of the polymer. The behaviour is attributable to the intermolecular interaction or entanglement, increasing the effective macromolecule dimensions and molecular weight. As a result of rheology of hydrated product, the swollen particles show coalescence. This results in a continuous viscoelastic matrix that fills the interstices, maintaining the integrity of the tablet, and retarding further penetration of the dissolution medium.

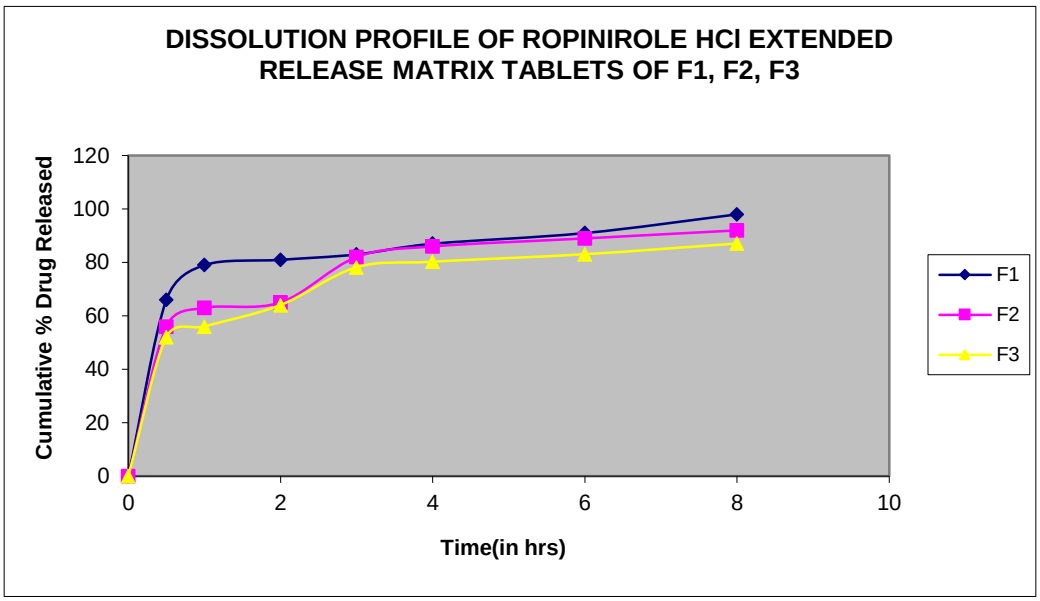

Fig. 1: Dissolution profiles of formulations: F1,F2,F3

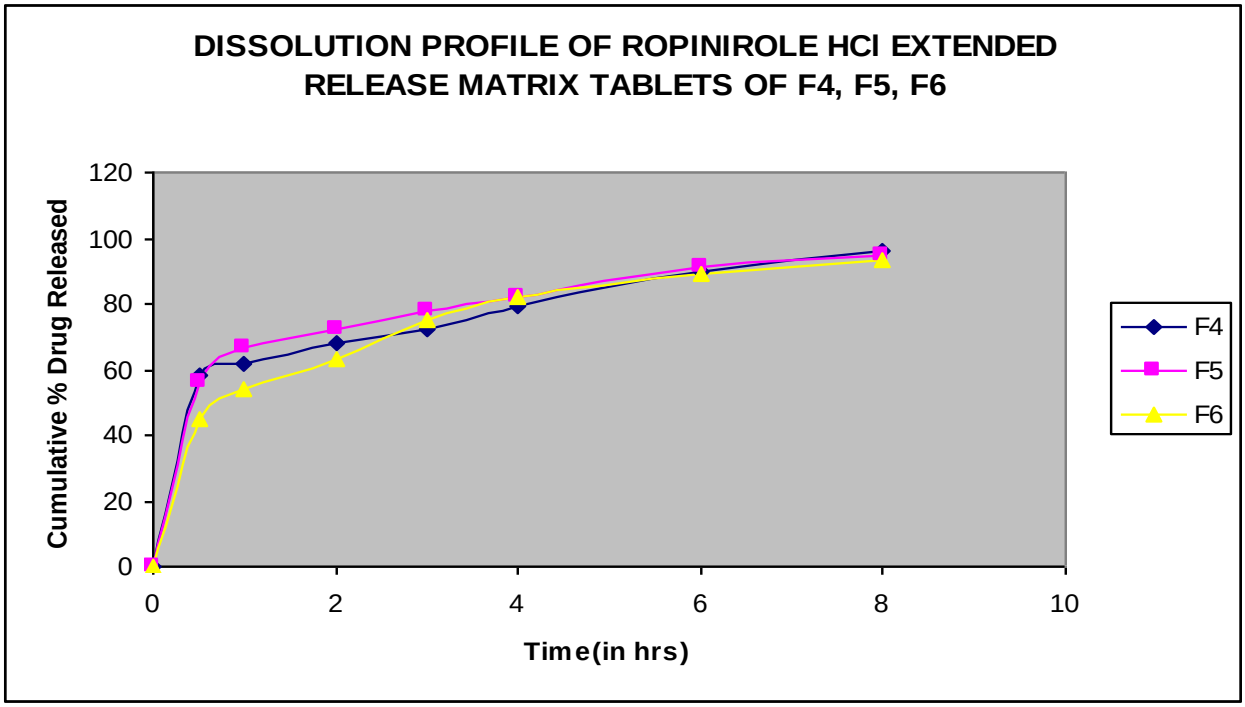

Fig. 2: Dissolution profiles of formulations: F4,F5,F6.

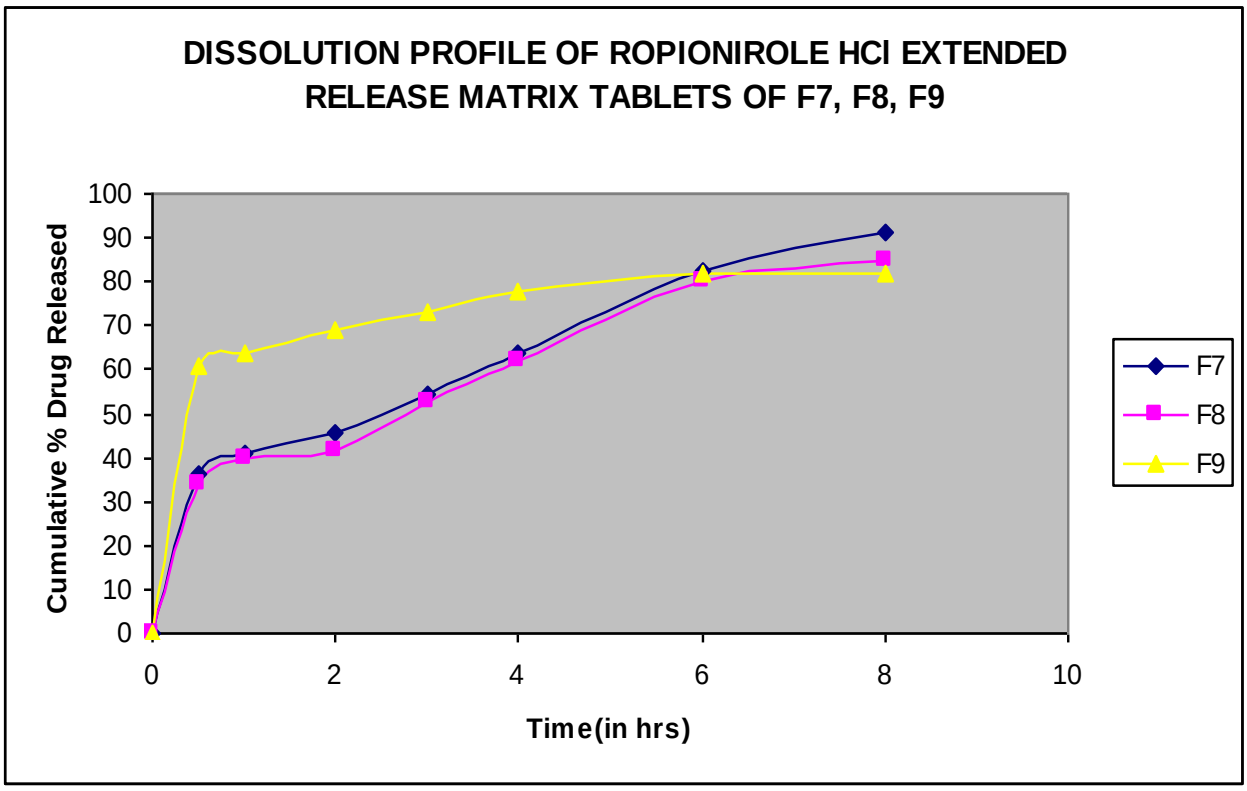

Fig. 3: Dissolution profiles of formulations: F7,F8,F9.

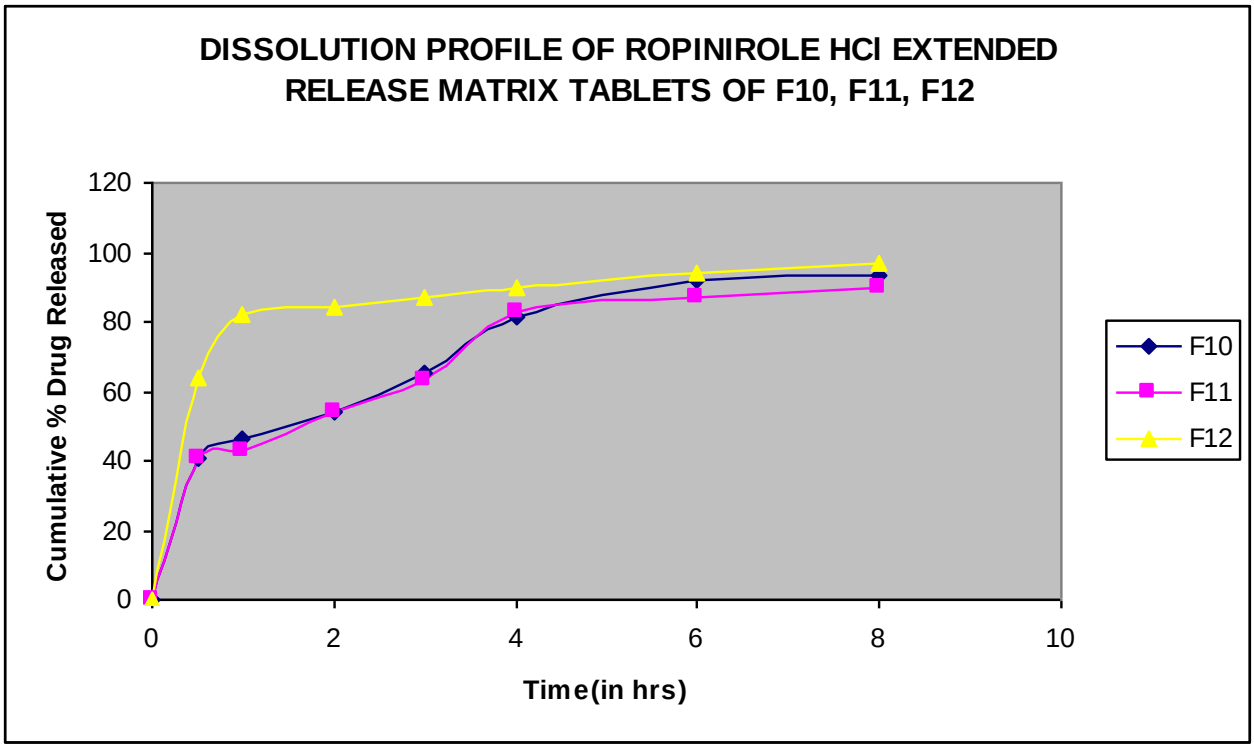

Fig. 4: Dissolution profiles of formulations: F10,F11,F12.

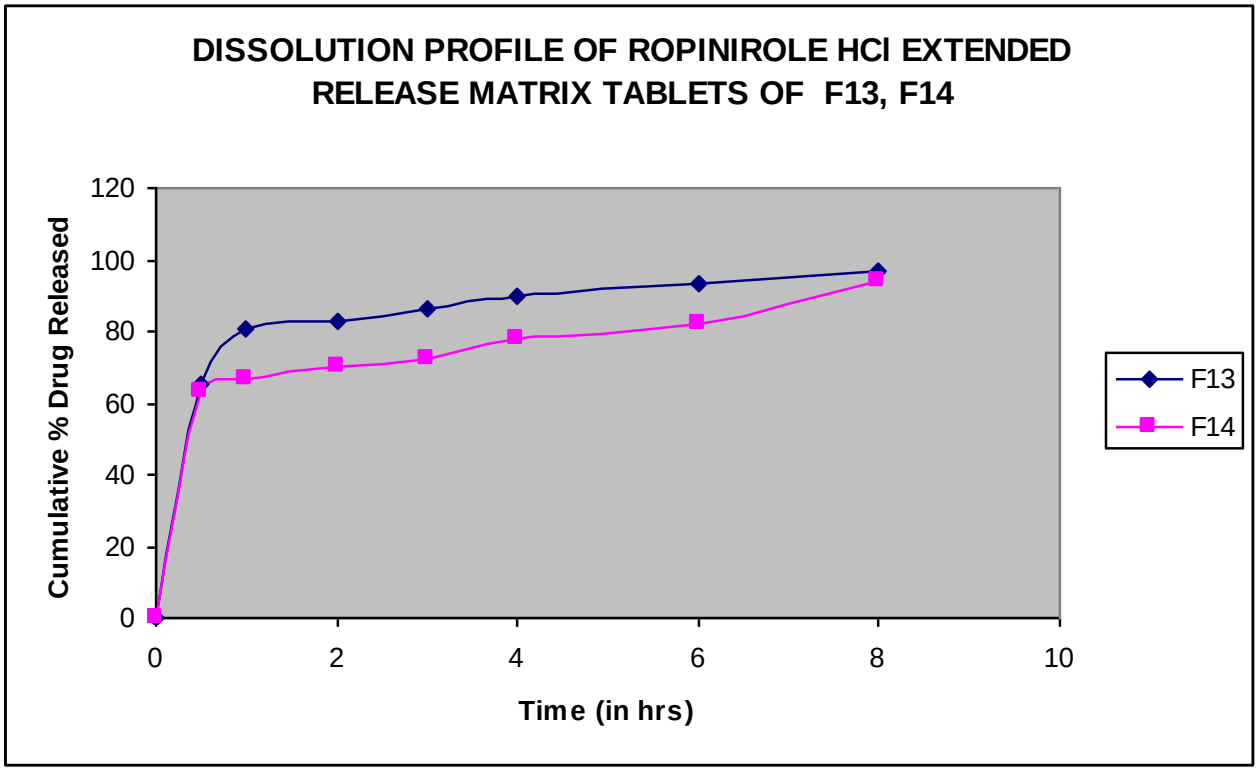

Fig. 5: Dissolution profiles of formulations: F13,F14.

Release Kinetics: The values of regression coefficients(r^2)and release rate constant (K) of all the formulations are represented in table 7a and 7b.The values of diffusion exponent (n)of the different formulationsare presented in table 7b.The drug release from

the formulations: F1,F2,F3,F7,F8, F10,F11,F12,F13 followed first order kinetics as the values of regression coefficient (r^2)for these batches was >0.9.The drug release from the batches:F1,F2,F3,F6,F7,F8,F9,F10,F11,F12 depends on diffusion and erosion mechanism, as the higuchiplot, for these batches showed the r^2 value >0.9. The values of, n ,of the different formulations ranged from 0.2399-0.6094.Based on n (table 7b) values, the drug release from the batches:F1,F2,F3,F4,F5,F6,F10,F14 exhibited fickian diffusion(n<0.45).However, the drug release from the formulations :F7,F8,F9,F11,F12,F13 demonstrated non-fickian diffusion(n>0.45).The drug release from the optimized formulation(F7) obeys first order kinetics(r^2 = 0.9603). Also, the drug release from the F7 batch depends on diffusion and erosion mechanism, as the higuchi plot showed an r^2 value(table 7a) of 0.9706.To ascertain the mechanism of release, the dissolution data was fitted in to the Peppas equation or the power law. Here, the value of the exponent "n" which is obtained from the slope of the graph of log Q (amount of drug dissolved) versus log t (time) yielded the value of 0.4694.Hece, the drug release from the F7 batch follows non-fickiandiffusion(table 7 b).

Table 7a: Drug Release Kinetics of Matrix Tablets

Batch	Zero Order		First Order		Higuchi Plot	
	r^2	K_0(mg/hr)	r^2	K_1(hr^{-1})	r^2	K_h
F1	0.8632	3.82	0.9796	0.089	0.9838	18.97
F2	0.8435	3.76	0.9566	0.084	0.9658	18.68
F3	0.8659	4.23	0.9473	0.163	0.9868	21.01
F4	0.2771	2.71	0.3231	0.128	0.5849	17.77
F5	0.5521	3.31	0.7207	0.087	0.8281	18.82
F6	0.8299	1.83	0.8812	0.024	0.9829	9.31
F7	0.9132	3.03	0.9603	0.051	0.9706	14.52
F8	0.9256	2.06	0.964	0.027	0.9935	9.911
F9	0.8433	1.75	0.8833	0.022	0.9811	8.799
F10	0.8118	3.83	0.9687	0.093	0.9789	19.538
F11	0.8934	4.06	0.9484	0.088	0.9692	23.946
F12	0.8362	4.81	0.9956	0.164	0.9091	25.064
F13	0.6996	4.73	0.9006	0.251	0.7049	20.92
F14	0.4162	3.462	0.4495	0.139	0.9593	19.669

* r^2 = Correlation coefficient; K = Kinetic constant

Table 7b: Drug Release Kinetics Of Matrix Tablets

Batch	Korsemeyer-Peppas	
	r^2	n
F1	0.9704	0.4069
F2	0.9429	0.4226
F3	0.9641	0.3726
F4	0.6135	0.0581
F5	0.9112	0.2516
F6	0.9978	0.3869
F7	0.9586	0.4694
F8	0.9848	0.6603
F9	0.9743	0.5629
F10	0.9936	0.4132
F11	0.9836	0.5836
F12	0.9601	0.6094
F13	0.9272	0.4573
F14	0.6891	0.2399

* r^2 = Correlation coefficient; n = Diffusion exponent

FTIR studies: The FTIR studies of the pure drug, polymers(sodium alginate, guar gum),drug-sodium alginate physical mixture and the drug-guar gum physical mixture was carried out to

study the interaction between the drug and the polymer. The FTIR spectrum of the pure drug shows the characteristic FTIR peaks at 3416cm^{-1} (N-H stretching), 1631cm^{-1}(C=C stretching),3076cm^{-1}(aromatic, C-Hstretching),2938cm^{-1} and 2881cm^{-1}(aliphatic C-H stretching),1312cm^{-1} and 1351cm^{-1} (C-N stretching),1758cm^{-1}(C=O stretching).The FTIR spectrum of the pure drug (alone), polymers (sodium alginate or guar gum), the drug: sodium alginate physical mixture and the drug-guar gum physical mixture are depicted in the Fig.6a-6e. The FTIR studies indicated that the drug (ropinirole hydrochloride) is compatible with guar gum and sodium alginate. All the peaks of the drug were observed in the drug-polymer (guar gum or sodium alginate) physical mixture, there by ruling out the drug-polymer interaction (Fig.6a-6e).

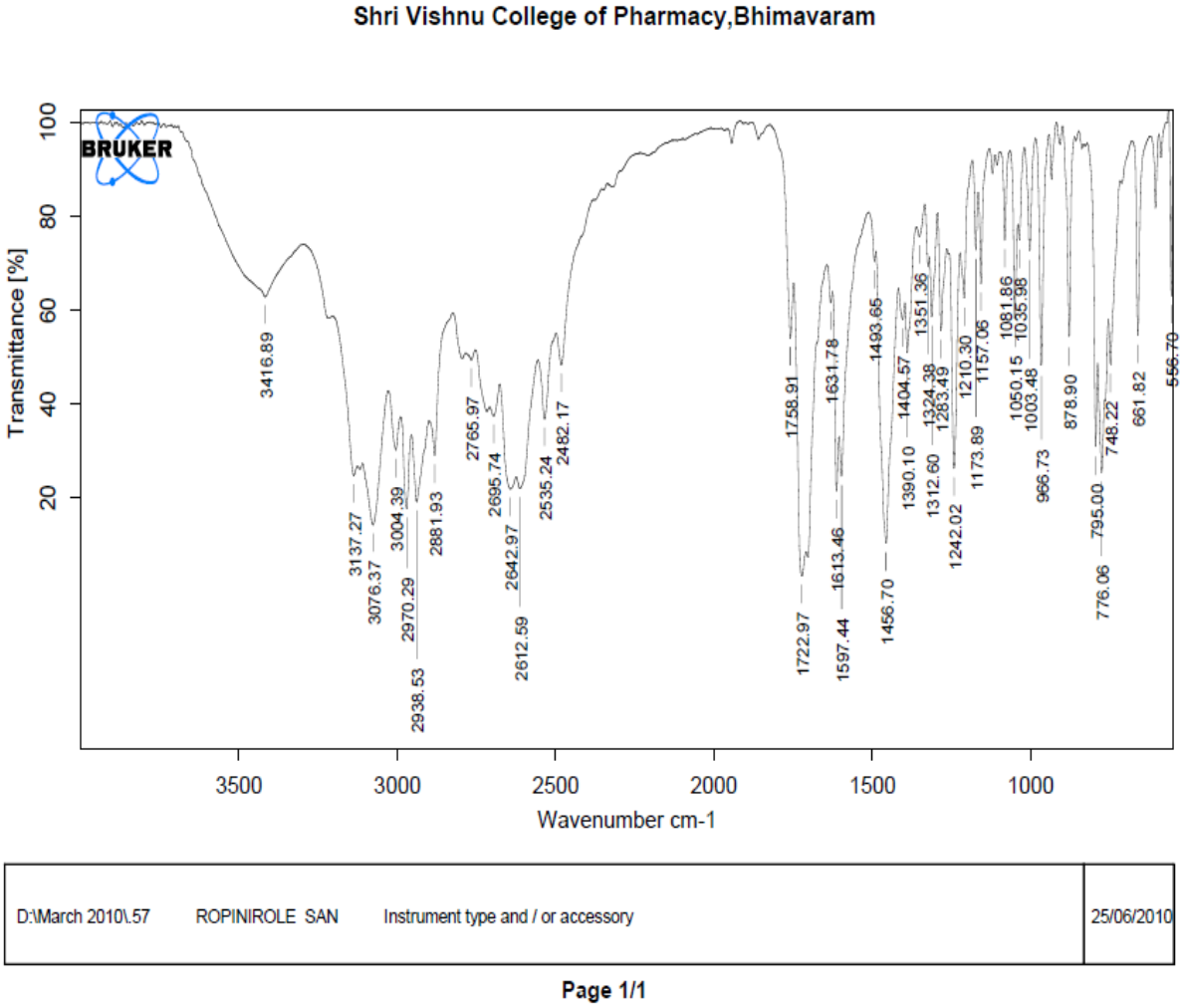

Fig.6a: FTIR spectrum of RopiniroleHCl

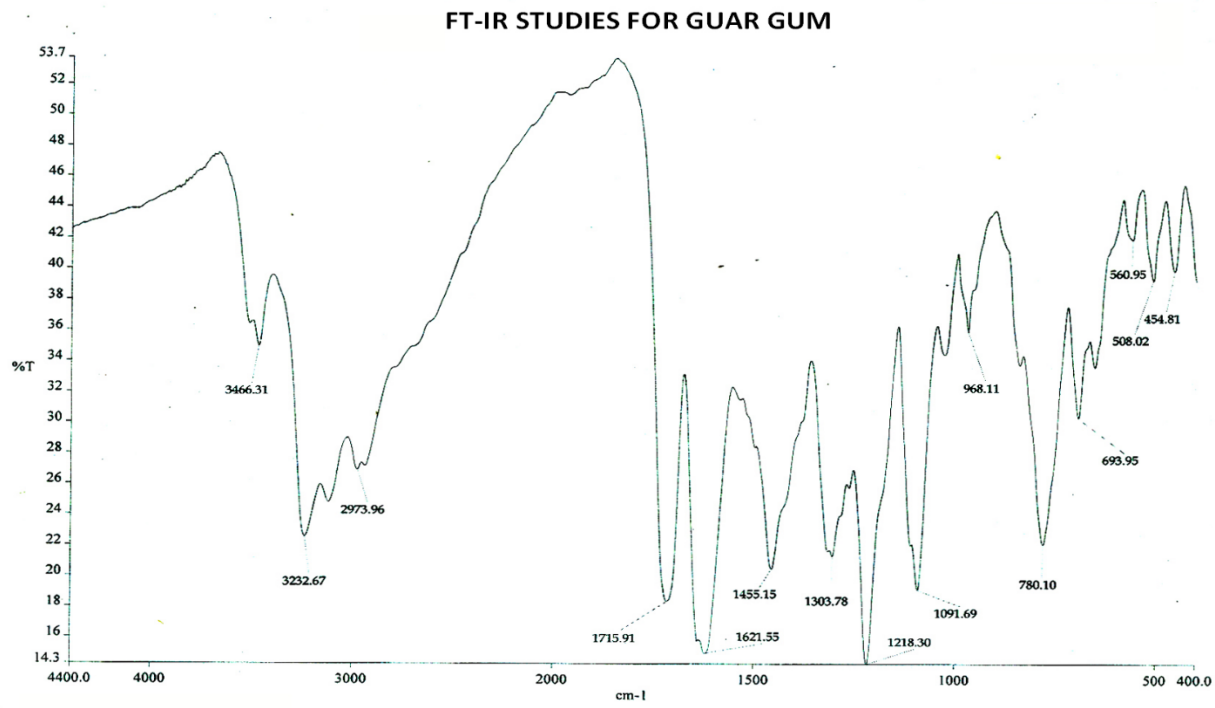

Fig.6b: FTIR spectrum of guar gum

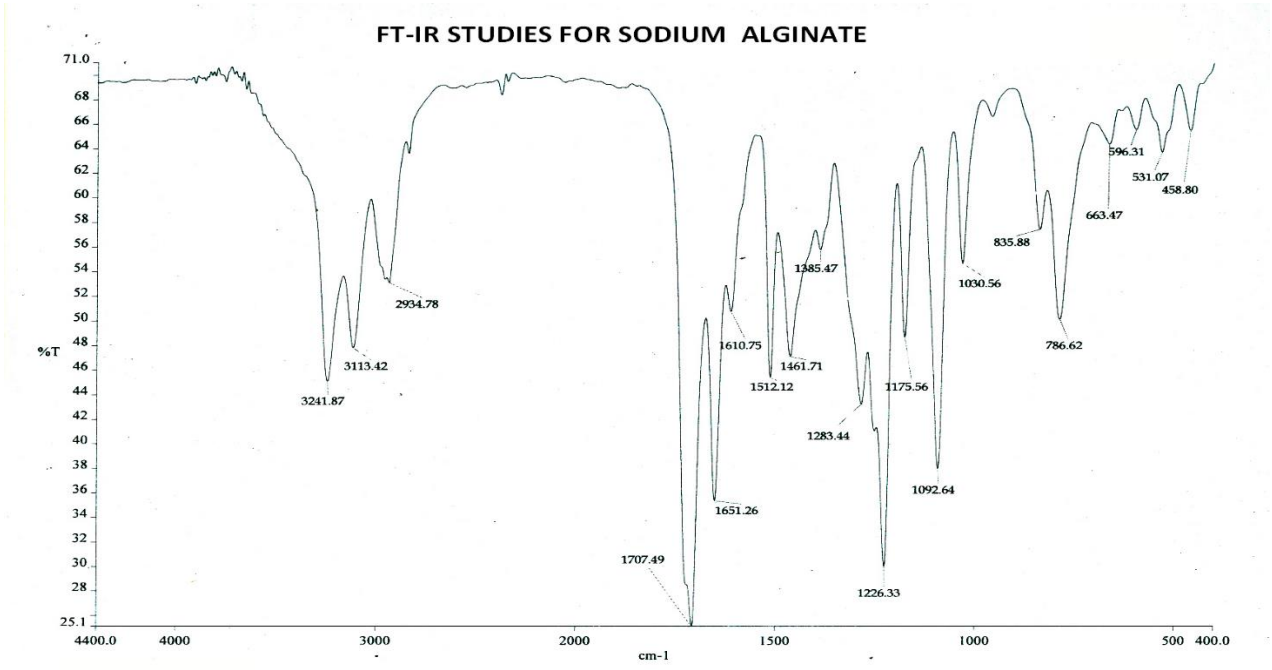

Fig.6c: FTIR spectrum of Sodium alginate

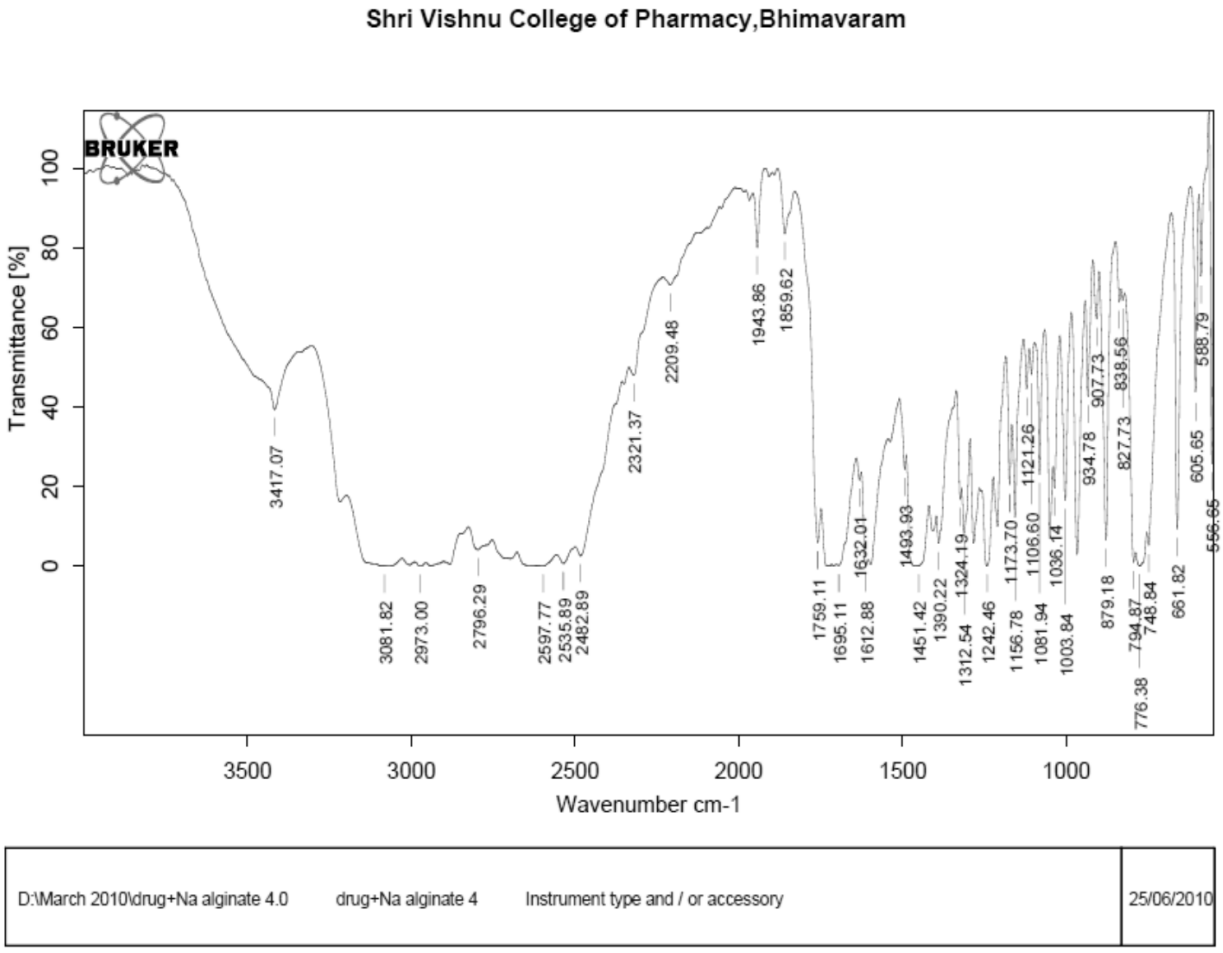

Fig.6d: FTIR spectrum of RopiniroleHCl+Sodium Alginate physical mixture

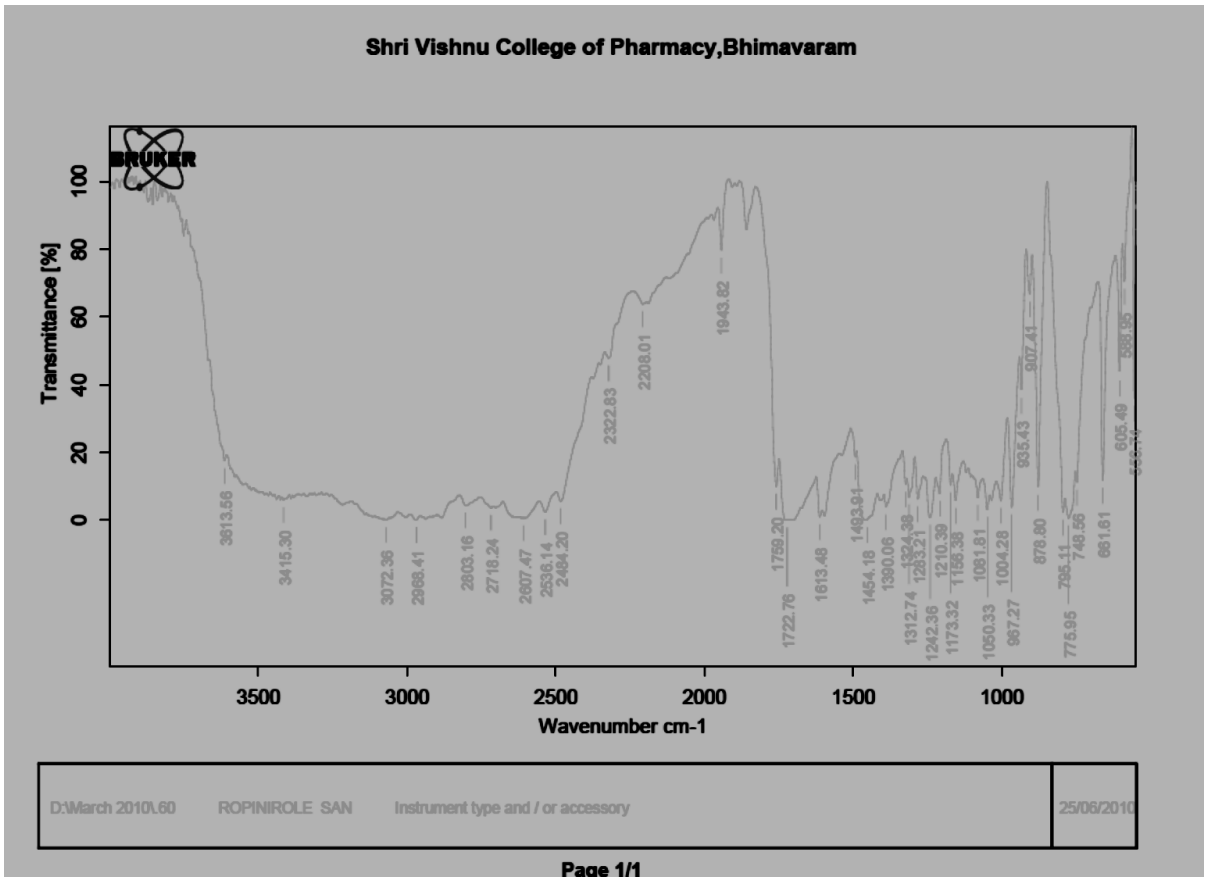

Fig.6e: FTIR spectrum for RopiniroleHCl+Guar gum physical mixture

CONCLUSION

A new oral drug delivery system for the controlled release of ropiniroleHCl was developed. The present study demonstrated the successful preparation of controlled release matrix tablets for water soluble drug (ropiniroleHCl) using direct compression and Wet granulation technology. The FTIR studies revealed the absence of drug-polmerinteraction. The formulation F7 (drug:guar gum,1:2.5), prepared by using the direct compression technique is the optimized formulation, it was able to control the drug release up to 8 hours. The formulated controlled release tablets can decrease, the frequency of drug administration and it can decrease the plasma drug fluctuation and it can improve the patient compliance.

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