ISSN (Online) 2249-6084 (Print) 2250-1029

International Journal of Pharmaceutical and Phytopharmacological Research (eIJPPR)
[Impact Factor – 0.852]

Journal Homepage: www.eijppr.com

Research Article

Formulation and Evaluation of Sustained Release Matrix Tablets of Quetiapine Fumarate

C H.Praveen Kumar[1], M. Nalini Krishna Reddy*[1], Namany Archana[2]
Department of Pharmaceutics, 1.Talla Padmavathi Pharmacy College, 2. Talla Padmavathi College of Pharmacy, Urus Kareemabad, Warangal, Telangana, India.

Article info

Article History:
Received 18 November 2014
Accepted 30 December 2014

Keywords:
Hydroxy Propyl Methyl Cellulose, Matrix tablets, Quetiapine fumarate, sustained release.

Abstract

The objective of this present investigation was to develop matrix tablets of Quetiapine fumarate(QF) for sustained release(SR). Different batches of Quetiapine fumarate sustained release tablets were prepared by direct compression technique using different polymers and to elucidate the release pattern of drug from SR matrix tablets, and compare with the theoretical sustained release profile. Xanthan gum, guar gum, karaya gum were used as natural polymers and HPMC K15,HPMC K100, Ethyl cellulose, Sodium CMC were used as synthetic polymers and by comparing the combination of different polymers was found to provided better-controlled release characteristics with excellent drug release. The prepared tablets were evaluated for weight variation, friability, hardness, thickness and in vitro dissolution studies. From the In vitro dissolution studies it is clear that as the concentration of polymer increased, drug release was found to be retarded. Formulation Q1and Q15 gave better-controlled drug release in comparison to the other formulations. FTIR study of pure Quetiapine fumarate and formulations showed that there is no drug polymer interaction.

1. INTRODUCTION

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms[1-8]. Oral controlled release drug delivery is a system that provides continuous oral delivery of drugs at predictable and reproducible kinetics for a predetermined period throughout the course of GI transit and also the system that target the delivery of a drug to a specific region within the GI tract for either a local or systemic action[3,4,9-12]. Sustained-release systems include any drug-
delivery system that achieves slow release of drug over an extended period of time. If the systems can provide some control, whether this be of a temporal or spatial nature, or both, of drug release in the body, or in other words, the system is successful at maintaining constant drug levels in the target tissue or cells, it is considered a controlled-release system[5,6,13-16].

Quetiapine Fumarate (QF) is an atypical anti-psychotic agent, widely used for bipolar disorder as well as schizophrenia management. Quetiapine fumarate (QF) (bis [2-(2-[4-(dibenzo[b,f][1,4]thiazepin-11-yl)]ethoxy)ethanol] fumarate, a dibenzothiazepine derivative, is a recent antipsychotic drug with an atypical neuropharmacological profile. Quetiapine is the antipsychotic that has the highest serotonin/dopamine binding ratio, being the serotonin type 2(5-HT2)-receptor blocking effect about twice as strong as the dopamine D2-receptor blocking effect . Due to this binding pattern, quetiapine causes minimal extrapyramidal side effects. It is readily absorbed from the gastrointestinal track with oral bioavailability of about 83% and a plasma elimination half life ranging from 6-7hours[17-25]. Administration of QF in the sustain release dosage form as once daily would be more desirable as this formulation is intended to be given to schizophrenic patients and moreover there was no litereature available for sustained release matrix formulation of Quetiapine Fumarate using HPMC K15M and HPMC K100M.[25-32]

Thus, an attempt has been made to formulate the sustained release matrix tablet dosage forms of Quetiapine Fumarate using various low-density and natural polymers.

Corresponding Author:
M. Nalini Krishna Reddy
Department of Pharmaceutics,
Talla Padmavathi Pharmacy College,
Warangal – 506001, India
Email: mnalinireddy84@gmail.com

2. MATERIALS AND METHODS

2.1 Materials

Quetiapine Fumarate was obtained as a gift sample from Dr. Reddy's Pharmaceuticals, Hyd and other excipients HPMC K100M , HPMC K15M obtained as a gift sample from Dr. Reddy's Pharmaceuticals, Hyd and Karaya gum and Xanthum gum purchased from Himedia Laboratories, Mumbai; Guar gum from Qualikems Pvt. Ltd. All other chemicals and reagents were of analytical grade and used without any further purification.

2.2 Spectrophotometric detrmination of quetiapine fumarate

The standard graphs and whole analysis was performed in the ionized water, USP P^H 1.2 (0.1N HCl). The wavelength selected was 250nm.

2.3 Construction of Theoretical release profile

Theoretical release profile of a drug is constructed when marketed preparations are not available, in order to check whether the formulations are releasing the drug similar to the predicted profile. Theoretical release profile of a drug is plotted on the basis of the loading dose and the drug availability rate.

The total dose of Quetiapine fumarte for sustained release formulation was calculated by the following equation

Dt = Dose (1+0.693 X t/ $t_{½}$)

Where, Dt = total dose of drug (40mg)

Dose= dose of immediate release part

t = time during which sustained release is desired i.e. 24hr

$t_{1/2}$ = half life of the drug (6hr)

The results are shown in table 3.

2.4 FORMULATION METHOD

Different formulations of Quetiapine fumarate were prepared by direct compression method using varying proportion of polymers either alone or in combination. The composition of various formulations of the tablets are listed in table. Calculated amount of the drug, polymers and filler (Avicel 102) was mixed thoroughly. Then the lubricated blend was added and subjected to compression

on a sixteen station rotary tablet punching machine using 9mm circular standard flat faced punches. The tablet weight was fixed for 300 mg. The formulation composition is shown in table 1.

Table 1: Composition of formulations of sustain release tablets of Quetiapine Fumarate

Formulations	Quetiapine Fumarate	HPMC K100M	HPMC K15M	EC	Xanthan gum	Guar gum	Karaya gum	SCMC	Avicel P^H102	Talc	Magnesium stearate
Q1	50	150		-	-	-	-	-	92	4	4
Q2	50	175		-	-	-	-	-	67	4	4
Q3	50	200		-	-	-	-	-	42	4	4
Q4	50	150		50	-	-	-	-	92	4	4
Q5	50	150		-	50	-	-	-	92	4	4
Q6	50	150		-	-	50	-	-	92	4	4
Q7	50	150		-	-	-	50	-	92	4	4
Q8	50	150		-	-	-	-	50	92	4	4
Q9	50	-	150	-	-	-	-	-	92	4	4
Q10	50	-	175	-	-	-	-	-	92	4	4
Q11	50	-	200	-	-	-	-	-	92	4	4
Q12	50	-	150	50	-	-	-	-	92	4	4
Q13	50	-	150	-	50	-	-	-	92	4	4
Q14	50	-	150	-	-	50	-	-	92	4	4
Q15	50	-	150	-	-	-	50	-	92	4	4
Q16	50	-	150	-	-	-	-	50	92	4	4

All the weights of ingredients are taken in mg.

2.5 Evaluation of matrix tablet

The physical properties such as friability, weight variation, thickness, and assay of compressed matrix tablet for each formulation were determined. Preweighed, randomly selected twenty tablets were placed in a Roche friability tester and operated for 4 min at 25 rpm. Compressed tablets should not lose more than 1% of their weigh. The thicknesses of tablets was measured by Vernier callipers (Mitatoyo, Japan). The drug content in terms of assay of each batch was determined in triplicate and all the results of these were shown in table 4.

***2.6 In vitro* drug release studies**

The release rate of matrix tablets of Quetiapine Fumarate was determined using USP Type 2 Apparatus. The dissolution test was performed in triplicate, using 900ml of 0.1 N HCl at 37±0.5˚C at 50 rpm for 24 hrs. A 5ml sample was withdrawn from the dissolution apparatus at specified time points and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45-µm membrane filter and diluted if necessary. Absorbance of these solutions was measured at specified wave length of 250nm by U.V-Visible Spectrophotometer.

2.7 Kinetic analysis of dissolution data

To analyze the in vitro release data various kinetic models were used to describe the release kinetics. The zero order rate describes the systems where the drug release rate is independent of its concentration The first order describes the release from system where release rate is concentration dependent. Higuchi described the release of drugs from insoluble matrix as a square root of time dependent process based on Fickian diffusion. Korsmeyer–Peppas model described mechanism of drug release from a polymeric system.

2.8 Calculation of similarity factor (f2)

Different dissolution profiles were compared to establish the effect of formulation or process variables on the drug release as well as comparison of test formulations to the theoretical release profile. The data were analyzed by the following formula.

f2 = 50 log {[1+ (1/N) ∑ (Ri – Ti)2]-0.5 x 100}

Where N = number of time points

Ri = % release from marketed product or Theoretical release profile

Ti = % release from test formulation at time i

If f2 value is in between 50-100, it is to be considered that 2 products share similar drug release behaviors.

2.9 Drug-excipient compatibility studies

2.9.1 Fourier Transform Infrared (FTIR) Spectroscopy

To investigate the possibility of chemical interaction between drug and polymer, FTIR spectra of pure QF, pure polymers and optimised formulations were analyzed over the range 400–4000 cm^{-1}. The result was shown in fig 6,7.

2.9.2 Differential Scanning Calorimetry (DSC

DSC study was conducted on Pure drug and two optimized formulations containingHPMC K100M, combination of HPMC K15M and karaya gum respectively. DSC thermogram of pure drug (Quetiapine fumarate) exhibits maximum peak at 178.1^0 C. The results were given in fig 8.

3. RESULTS AND DISCUSSION

3.1 Standard graph of Quetiapine fumarate in 0.1NHCl at 250nm

The standard graph of Quetiapine fumarate in 0.1N HCl showed a good linearity with R^2 of 0.9989, in the concentration range of 0-30 µg/ml.

Table 2: Calibration data

Concentration (µgm/ml)	Absorbance
0	0
5	0.185
10	0.326
15	0.486
20	0.625
25	0.779
30	0.927

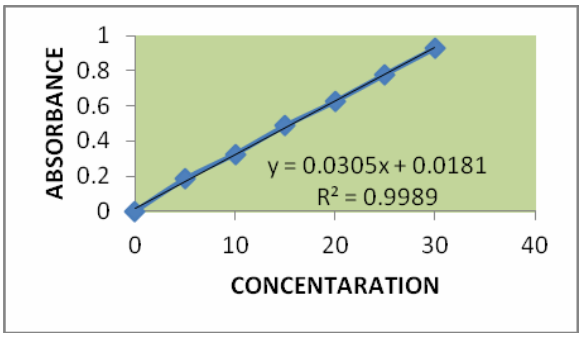

Fig 1: Standard graph of Quetiapine fumarate

Table 3: Theoretical release profile of Quetiapine fumarate

Time in hrs to be released	Amount of Quetiapine fumarate (mg)	% drug released
0	0	0
1	13.25	26.51
2	14.84	29.68
4	18.02	36.04
6	21.2	42.4
8	24.38	48.76
10	27.56	55.12
12	30.74	61.48
20	43.46	86.92
24	49.82	99.64

3.2 Evaluation of the quetiapine fumarate tablets for physical parameters

The Hardness of the tablets was found in the range of 4.0-5.5 Kg/cm^2 indicating satisfactory mechanical strength. The thickness of the tablets was found to be between3.50 and 3.84mm. The friability was below 1% for all the formulations, which is an indication of good mechanical resistance of the tablet. Assay of the prepared matrix tablets was found in the range of 98-100%.clearly indicating the good content uniformity. This study indicated that all the prepared formulations were good.

Table 4: Physical parameters of the prepared formulation

Formulation code	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Assay (%)
Q1	350±3	4.5±0.3	3.84±0.05	0.32±0.04	98.23±0.89
Q2	348±2	4.6±0.5	3.76±0.06	0.19±0.05	99.65±0.68
Q3	346±3	5.0±0.5	3.50±0.04	0.29±0.06	98.45±0.47
Q4	347±2	4.0±0.5	3.76±0.04	0.33±0.06	98.44±0.69
Q5	348±3	4.5±0.2	3.63±0.06	0.29±0.07	99.23±0.53
Q6	349±3	4.2±0.5	3.50±0.04	0.29±0.03	98.45±0.42
Q7	346±2	4.5±0.4	3.86±0.03	0.26±0.04	99.12±0.39
Q8	348±2	5.0±0.2	3.5520.06	0.23±0.07	98.65±0.78
Q9	343±3	5.2±0.5	3.50±0.04	0.29±0.08	98.45±0.67
Q10	347±3	5.5±0.5	3.50±0.04	0.29±0.05	98.45±0.54
Q11	344±3	5.0±0.5	3.50±0.04	0.29±0.03	98.45±0.65
Q12	348±2	4.5±0.2	3.60±0.04	0.24±0.07	99.72±0.52
Q13	343±2	4.2±0.5	3.50±0.04	0.29±0.05	98.45±0.46
Q14	345±2	4.2±0.5	3.76±0.06	0.19±0.04	99.65±0.76
Q15	350±3	5.0±0.5	3.50±0.04	0.29±0.07	98.45±0.86
Q16	348±3	5.2±0.5	3.50±0.04	0.29±0.06	98.45±0.65

***3.3 In vitro* drug release studies of quetiapine fumarate matrix tablets**

All the matrix formulations Q1-Q16 showed the drug release up to 24 hrs in controlled manner without changing their physical integrity in dissolution medium. The In Vitro dissolution data was fitted to different kinetic models such as Zero order, First order, Higuchi and Korsmeyer-peppas equation. All the release profiles of 16 formulations were given in fig. below.

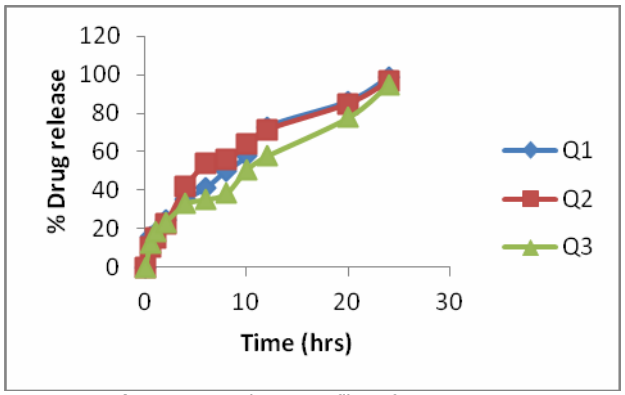

Fig: 2: Drug release profiles of Q1, Q2, Q3

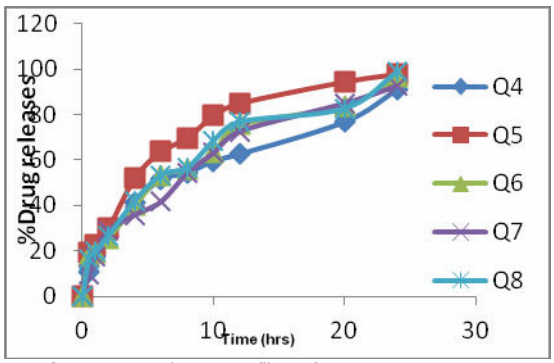

Fig 3: Drug release profiles of Q4, Q5, Q6, Q7, Q8

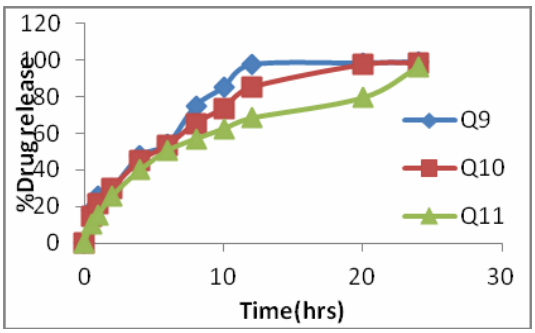

Fig 4: Drug release profiles of Q9, Q10, Q11

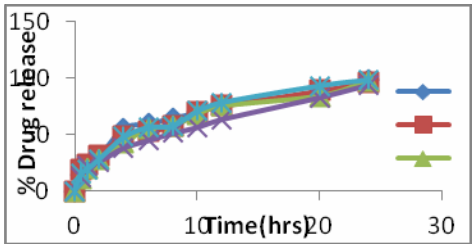

Fig 5: Drug release profiles of Q12, Q13, Q14, Q15, Q16

Table 5: Cummulative percentage drug release for 24 hours

Formulation	Time(hrs)									
	0	1	2	4	6	8	10	12	20	24
Q1	0	17.82±1.35	24.54±1.46	35.17±0.85	41.31±1.67	50.22±1.54	57.83±0.98	72.53±1.76	86.10±1.89	98.50±0.90
Q2	0	15.40±1.25	22.60±1.86	42.07±2.13	53.64±1.28	56.01±0.68	63.68±1.53	71.35±1.67	84.92±2.41	96.50±1.46
Q3	0	18.82±1.05	23.48±1.10	33.10±0.98	35.23±1.97	38.41±2.14	50.75±1.69	57.78±2.65	77.84±0.67	94.96±1.27
Q4	0	17.76±1.43	26.43±1.20	41.36±1.48	51.40±1.59	54.24±1.13	59.55±1.07	62.50±1.66	76.660.35	90.83±1.10
Q5	0	22.83±3.12	30.15±2.61	52.11±0.87	63.68±1.70	69.58±1.59	79.61±1.06	84.92±1.27	94.37±1.31	97.80±1.35
Q6	0	19.12±1.37	25.49±1.24	40.13±0.53	53.23±1.24	56.01±1.11	63.09±1.19	75.48±1.91	83.74±0.89	96.73±0.24
Q7	0	17.76±1.46	28.74±1.34	35.82±1.64	41.66±0.45	54.24±0.77	63.09±0.67	72.53±1.31	84.92±1.21	92.60±1.36
Q8	0	19.71±1.11	26.85±1.18	42.01±0.68	53.29±0.96	56.60±0.21	68.40±1.28	76.66±1.31	82.56±1.38	98.68±0.43
Q9	0	25.37±0.98	29.68±1.32	47.50±1.28	54.05±1.57	74.89±1.44	84.92±1.24	97.32±1.68	98.25±0.55	98.89±0.54
Q10	0	21.48±0.86	30.03±1.81	44.91±2.04	53.52±2.33	65.45±1.08	73.71±1.54	84.92±1.32	97.32±0.89	98.34±0.86
Q11	0	15.34±1.24	25.84±1.07	39.95±1.11	50.75±2.08	57.06±1.53	62.50±0.86	68.40±1.11	79.61±1.45	96.50±1.12
Q12	0	19.88±1.13	33.39±1.21	55.76±0.65	59.55±0.75	64.86±1.32	69.58±1.51	76.66±1.34	87.29±1.11	98.78±0.46
Q13	0	23.25±1.30	32.04±1.81	48.51±0.78	53.64±1.35	57.19±1.51	69.58±1.21	75.48±1.19	89.06±1.36	96.73±1.12
Q14	0	20.24±0.98	27.97±1.28	42.60±1.34	55.76±0.56	57.78±1.98	68.40±0.77	75.48±1.31	84.33±0.89	97.35±0.64
Q15	0	22.42±1.23	26.20±1.11	38.47±1.45	44.96±0.86	51.46±0.87	58.60±1.98	63.68±1.36	83.15±1.23	94.37±1.54
Q16	0	19.29±1.43	28.56±0.94	47.97±1.78	56.47±1.64	57.78±1.34	70.76±1.76	78.43±1.47	93.19±0.89	98.50±0.23

The formulations Q1, Q3, Q6, Q8, Q11, Q14 and Q15 followed Zero order kinetics as indicated by their high regression values compared to first order kinetics whereas formulation Q2, Q4, Q5, Q7, Q9, Q10, Q12, Q13 and Q16 followed first order kinetics. All the formulations (Q1 to Q16) showed good correlation in Higuchi kinetics clearly indicating that the drug release mechanism was predominantly diffusion controlled. Peppas release exponent (n)values indicated that the drug release from formulations Q1,Q2, Q6, Q7, Q8, Q11 and Q16 followed non-fickian diffusion (n>0.5) whereas formulation Q3, Q4, Q5, Q9, Q12, Q13, Q14 and Q15 followed Fickian diffusion (n<0.5).

The f2 values for all the formulations were higher than 50 indicating the sameness of release profiles.

Table 6: Regression coefficient (R^2) values of all formulations for different kinetic models

Formulation code	Zero order R^2	First Order R^2	Higuchi R^2	Korsmeyer R^2	Korsmeyer n	Similarity factor f2
Q1	0.966	0.863	0.986	0.990	0.545	64.062
Q2	0.907	0.927	0.982	0.977	0.576	54.725
Q3	0.990	0.865	0.954	0.954	0.497	58.514
Q4	0.917	0.938	0.980	0.983	0.490	57.79
Q5	0.816	0.993	0.939	0.964	0.481	39.462
Q6	0.915	0.911	0.981	0.988	0.518	55.430
Q7	0.935	0.984	0.984	0.985	0.518	60.060
Q8	0.901	0.828	0.974	0.986	0.508	52.64
Q9	0.780	0.917	0.898	0.949	0.489	36.019
Q10	0.882	0.982	0.970	0.987	0.505	44.306
Q11	0.934	0.874	0.982	0.982	0.550	57.099
Q12	0.851	0.859	0.951	0.954	0.483	44.92
Q13	0.921	0.956	0.986	0.990	0.447	51.33
Q14	0.901	0.900	0.978	0.987	0.495	52.14
Q15	0.982	0.933	0.993	0.987	0.460	73.16
Q16	0.899	0.955	0.979	0.981	0.515	48.25

3.4 FTIR studies

The IR spectrum of pure QF showed strong absorption bands at wave numbers of 3284, 2941, 1741, 1597, 1371 and 1070 cm^{-1} due to –OH stretching, C-H bend in plane and C-C stretching respectively

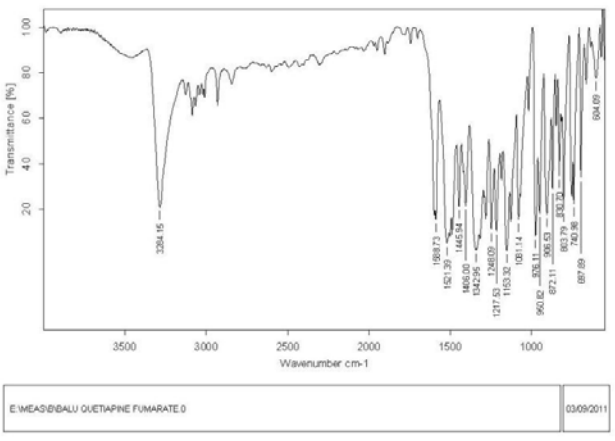

Fig 6: FT-IR Spectra of Quetiapine Fumarate

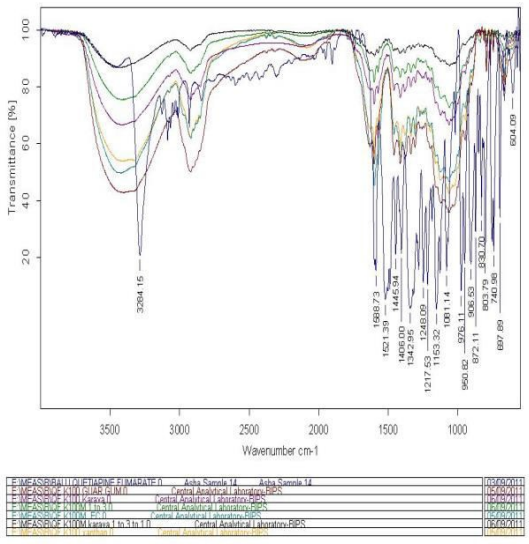

Fig 7: FT-IR Spectra of optimised formula

3.5 DSC studies

Similar peaks were observed for the formulation prepared with HPMC K100M at173.5^{O}C and at 171.2^{O}C for formulation prepared using HPMC K 15M and karaya gum. Polymers used in the optimized formulations can be considered compatible with Quetiapine fumarate as there was no much change in the drug peak.

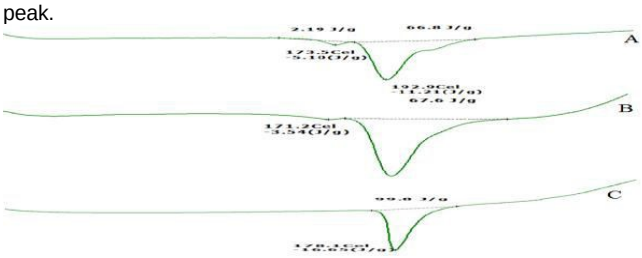

Fig 8: A) QF,HPMC K100M B) QF,HPMC K15,Karaya gum C) QF

4. CONCLUSION

Finally, concluded that different swelling polymers such as HPMC K100M, HPMC K15Mindividually and in combination with other polymers such as Xanthan gum, Guar gum,karaya gum, Sodium CMC and Ethyl cellulose can be successfully employed in the preparation of sustained release tablets of Quetiapine Fumarate. The research study provided useful information for the formulation scientists on formulation, characterization during development of controlled drug delivery systems of Quetiapine Fumarate using these polymers.[33-37]

5. ACKNOWLEDGMENTS

Authors wish to thanks all research team members of Talla Padmavathi colleges of Pharmacy to carry out their work and proving necessity facilities.

REFERENCES

1. Controlled release of oral dosage forms Nandita G. Das and Sudip K. Das. Formulation,Fill & Finish 2003.2. Washington N, Washington C, Wilson CG, “Physiological Pharmaceutics-II”, Taylor andFrancis, New York, 2001.
2. Jain N K. “Advance in Controlled and Novel drug delivery”, CBS publisher and distributor, New Delhi, pg-76-95.
3. Chien Y. W., “Novel Drug Delivery system”, (2nd ed.), Marcel Dekker. 1992; 139-196.
4. Sanjay Garg and Shring Sharma., Drug Delivery Oral. business Briefing Pharmatech.2003.
5. Marvola M, Kannikoski A,et al., The effect of food on gastrointestinal transit and drug absorption of a multiparticular sustained-release Verapamil formulation. Int JPharm 1989; 53: 145-55.
6. Lenaerts VM, Gurny R. Bioadhesive Drug Delivery Systems, CRC Press, Boca Raton, F L, 1990.
7. Clarke GM, Newton J M, et al., Comparative gastrointestinal transit of pelletsystem of varying density. Int J Pharm 1995; 114: 1-11.
8. Chitnis VS, Malshe VS, et al., Bioadhesive polymers synthesis, evaluation and application in controlled release tablets. Drug Dev Ind Pharm 1991; 17: 879-92.
9. F. GarcõÂa-Ochoa,V.E. Santo, J.A. Casa, E, et al., Xanthan gum: production, recovery, and properties. Biotechnology Advances. 2000; 18: 549 ± 579.
10. Sakr FM. A programmable drug delivery system for oral administration. Int J pharm1999; 184: 131-9.
11. Rowe RC, Sheskey PJ, Weller PJ. Handbook of pharmaceutical excipients. 4th ed. (London): Pharmaceutical Press; 2003.
12. Peppas NA. Analysis of fickian and non-fickian drug release from polymers. PharmActa Helv. 1985;60:110-111.
13. A.Silvina, B.C.Maria, et al., Invitro studies of diclofenac sodium controlled release from biopolymeric hydrophilic matrices, J. Pharm.Sci. 2002, 5 (3), 213-219.
14. S.C. Basak, Y. Srinivasa Rao, et al., Controlled release HPMC matrix tablets of Propranol hydrochloride, Ind. Pharm. Sci. 2004, 66, 827.
15. Sharifi V, Bakhshaie J, Hatmi, Z, Faghih-Nasiri L, Sadeghianmehr Z, Mirkia S, Mirsharifa SM. Self-reported psychotic symptoms in the general population: Correlates in an Iranian Urban area. 2012. Psychopathology. 45(6), pp. 374-380.
16. Ashrafi MR, Salehi S, Malamiri RA, Heidari M, Hosseini SA, Samiei M, Tavasoli AR, Togha M. Efficacy and safety of cinnarizine in the prophylaxis of migraine in children: A double-blind placebo-controlled randomized trial. 2014. Pediatric Neurology. 51(4), pp. 503-508
17. Shushizadeh MR, Dalband N. SiO 2/H 2SO 4: An efficient catalytic system for solvent-free 1, 5-benzodiazepines synthesis. 2012. Jundishapur Journal of Natural Pharmaceutical Products. 7(2), pp. 61-64.
18. Moradian M. Diagnostic errors in echocardiography: Review of five interesting pediatric cases. 2012. Journal of Tehran University Heart Center. 7(1), pp. 33-36.
19. Moradian M, Nokhostin-Davari P, Merajie M, Pouraliakbar HR. Aortic runoff as a sign of intracranial arteriovenous malformation: Report of two cases. 2013. Iranian Journal of Pediatrics. 23(2), pp. 229-232.
20. Moradian M, Fard MZ, Mozaffari K. Atrial rhabdomyoma: A case report. Iranian Heart Journal. . 2014 15(2), pp. 39-42
21. Kocharian A, Shabanian R, Rahimzadeh M, Kiani A, Hosseini A, Zanjani KS, Heidari-Bateni G, Hosseini-Navid N. N-terminal Pro-B-type natriuretic peptide and ventricular dysfunction in children and adolescents. 2009. Cardiology in the Young. 19(6), pp. 580-588.
22. Taymoori P, Lubans D, Berry TR. Evaluation of the health promotion model to predict physical activity in iranian adolescent boys. Health Education and Behavior. 2010. 37(1), pp. 84-96
23. Piranfar MA, Karvandi M, YazdaniS, Pishgahi M, Mehdizadeh M, Hajfathali A, Tabarraee M. Bone marrow transplantation may augment cardiac systolic function in patients with a reduced left ventricular ejection fraction. Journal of Cardiovascular Disease Research. 2012. 3(4), pp. 310-314
24. Moshki M, Hassanzade T, Taymoori P. Effect of life skills training on drug abuse preventive behaviors among university students. International Journal of Preventive Medicine. 2014. 5(5), pp. 577-583
25. Taymoori P, Berry T, Roshani D. Differences in health beliefs across stage of adoption of mammography in Iranian women. Cancer Nursing. 2014. 37(3), pp. 208-217
26. Moazen B, Rezaei F, Lotfizadeh M, Darvishi M, Farzadfar F. Mind the gap in reporting the outdated statistics. Int J Health Policy Manag. 2014 Oct 2;3(5):295-6.
27. Mohaghegh Shalmani H, Noori A, Shokoohi M, Khajavi A, Darvishi M, Delavari A, Jamshidi HR, Naderimagham S. Burden of Hepatitis C in Iran Between 1990 and 2010: findings from the Global Burden of Disease Study 2010. Arch Iran Med. 2015 Aug;18(8):508-14.
28. Moradian M. Fetal circulation. Comprehensive Approach to Adult Congenital Heart Disease. 2014.pp. 13-17.
29. Assareh M , Moghaddam M F , Rakhshani T , Nikoo M A , Effatpanah M , Rai A , Rezaie L. The motives behind the decision for choosing self-immolation as a method for suicide. 2013. Life Science Journal. 10(4), pp. 1610-1614.
30. Semnani S, Roshandel G., Abdolahi N, Besharat S, Keshtkar AA, Joshaqani H, Danesh A. HBV/HCV co-infection in Iran: A seroepidemiological based study. 2006. Pakistan Journal of Biological Sciences. 9(13), pp. 2538-2540.
31. Aghamohammadzadeh N, Aliasgarzadeh A, Baglar L, Abdollahifard S, Bahrami A, Najafipour F, Niafar M. Comparison of metformin and cyproteroneestrodiol compound effect on hs c-reactive protein and serum androgen levels in patients with poly cystic ovary syndrome. 2010. Pakistan Journal of Medical Sciences. 26(2), pp. 347-351.
32. Moghadam MYA, Moradian M, Givtaj N, Mozaffari K. Intraluminal ascending aorta fibroma. 2011. Journal of Tehran University Heart Center. 6(1), pp. 45-47
33. Moradian M, Shahmohammadi A, Yoosefnia MA, Mozaffari K. One and a half ventricular repair for Uhl's anomaly with one year follow up. 2011. Iranian Cardiovascular Research Journal. 5(1), pp. 35-38
34. Shushizadeh MR, Mostoufi A, Fakhrian M. Marine sponge/cuo nanocrystal: A natural and efficient catalyst for sulfonamides synthesis. 2012. Jundishapur Journal of Natural Pharmaceutical Products. 7(4), pp. 134-139.
35. Taymoori P, Moshki M, Roshani D. Facilitator psychological constructs for mammography screening among iranian women. Asian Pacific Journal of Cancer Prevention. 2014. 15(17), pp. 7309-7316
36. Macooie AA, Pashapoor N, Yekta Z, Karamyar M. Serum prolactin level after febrile seizure versus epileptic seizure in 6-month-old to 5-year-old children. Iranian Journal of Medical Sciences. 2009. 34(3), pp. 177-180.
37. Nazer MR, Ghanadi K, Goodarzi G, Sajedi Y, PourniaY, Darvishi M. Prevalence of Chlamydia pneumoniae by Real time PCR in referred patients with respiratory syndrome to clinic center of infectious diseases. Life Science Journal. Volume 11, Issue 1 SPECL. ISSUE, 2014, Article number 15, Pages 87-92.