

DESIGN AND IN-VITRO CHARACTERIZATION OF QUETIAPINE FUMARATE GASTRO RETENTIVE FLOATING TABLETS

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ABSTRACT

Atypical antipsychotic drug quetiapine is used to treat schizophrenia, bipolar disorder, and major depressive disorder. Due to its sedative effect, it is frequently used as a sleep aid, however the advantages of doing so do not always seem to outweigh the drawbacks. It's consumed orally. The object of the present work is preparing Quetiapine fumarate gastro retentive floating tablets. With changing amounts of retardation polymers, the gas producing agent accural was introduced at various concentrations. Carbopol 971, Carbopol L934P and HPMCK100M were used as polymers for retardation. The formulation blend's various physicochemical properties were assessed, and all the parameters were found to be within the acceptable ranges. The formulations. F1-F9 were developed, and several quality control criteria were used to evaluate them. The formulations were developed, and several quality control criteria were used to evaluate them. According to the dissolution results, formulation F8 was the best, with a maximum percent drug release of 97.81% and a floating time of 12 hours.

KEYBOARDS: Quetiapine fumarate, gastro retentive floating tablets.

INTRODUCTION

Quetiapine fumarate is only moderately soluble in basic pH and extremely soluble in acidic pH. he medicine should be kept in the stomach for a longer amount of time to ensure optimum absorption and bioavailability. The solubility of quetiapine fumarate is pH dependent. In order to extend the period that the dose form remains in the stomach or upper gastrointestinal tract until the medicine is fully discharged from the system, a gastro retentive floating tablet is a preferred strategy. The aim of this study was to formulate and evaluate gastro retentive floating tablets of quetiapine fumarate.

MATERIALS

Quetiapine fumarate, Carbopol 971, Carbopol L934P, HPMCK100M, Accural, Magnesium stearate, Talc all

and microcrystalline cellulose were the substances, which were of laboratory standards.

METHODOLOGY

Formulation (Or) preparation of floating tablets of quetiapine fumarate

Optimization of accural concentration

As an effervescent gas generator, accural was used. It aids in the formulation's buoyancy. Different Accural concentrations were used, and floating lag time and floating duration were noted. Based on that, Accural's concentration was decided upon and prepared for further formulations.

Table 1: Optimization accural concentration.

S. No	Excipient Name	EF1	EF2	EF3
1	Quetiapine fumarate	100	100	100
2	HPMCK100	60	60	60
3	Accural	30	60	90
4	Mg.Stearate	3	3	3
5	Talc	3	3	3
6	MCC pH 102	Q.S	Q.S	Q.S

Table 2: Composition of floating tablets of quetiapine fumarate by using different concentrations of polymers.

Formulation No.	Quetiapinefumarate	Carbopol 971	Carbopo l L934p	HPMC K100M	Accural	Mag. Stearate	Talc	MCC pH 102
F1	100	30	-----	-----	60	3	3	QS
F2	100	60	-----	-----	60	3	3	QS
F3	100	90	-----	-----	60	3	3	QS
F4	100	-----	30	-----	60	3	3	QS
F5	100	-----	60	-----	60	3	3	QS
F6	100	-----	90	-----	60	3	3	QS
F7	100	-----	-----	30	60	3	3	QS
F8	100	-----	-----	60	60	3	3	QS
F9	100	-----	-----	90	60	3	3	QS

All the quantities were in mg

Method of Preparation

In this study, floating matrix tablets were created using the direct compression method of Quetiapine fumarate with Carbopol 971, Carbopol L934p, HPMC K 100M. Each ingredient was precisely weighed and put through mesh number 60. For 15 minutes, the medication and polymer were geometrically mixed in a mortar and pestle in order to completely combine the materials. Next, microcrystalline cellulose, accural, talc, and magnesium stearate were mixed one at a time. These components were fully combined before the powder mixture was run through # 40mesh. On a multi punch 8 station Rotary tablet compression machine (Cemach, machineries ltd,

lab press 8 station, India) employing 9mm flat round punches, tablets were compressed using the direct compression method.

Evaluation of post compression parameters for prepared tablets

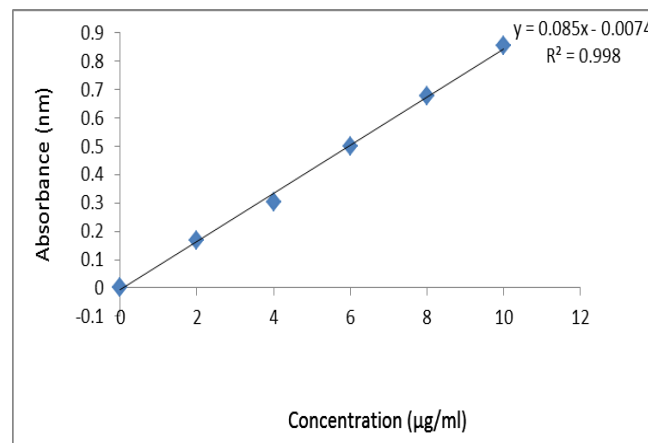
The physicochemical characteristics of the suggested formulation tablets, such as weight variation, hardness, thickness, friability, and drug content, were examined. Results and Discussion.

Standard Graph of Quetiapine in 0.1N HCl at 232 nm

The following table lists the quetiapine standard graph values:

Table 3: Standard graph values of quetiapine in 0.1N HCl at 232 nm.

Concentration (µg/ml)	Absorbance
2	0.169
4	0.301
6	0.498
8	0.678
10	0.853

**Fig. 1: Normative curve for quetiapine.**

Precompression quetiapine evaluation parameters floating formulation blend

The powder mixes were created by combining the different elements indicated and were used to characterise different powder flow qualities.

Bulk density

The bulk densities of all the formulations were determined to be between 0.52 and 0.56 (gm/cm³), demonstrating the powder's favourable flow characteristics.

Tapped density

All of the formulations' tapped densities were determined to be between 0.54 and 0.57, demonstrating the powder's favourable flow characteristics.

Compressibility index

All of the formulations' compressibility indices were found to range from 13.07 to 17.68, indicating that the powder had adequate flow characteristics.

Hausner's ratio

The hausner ratio ranges from 0.97 to 1.22 in all formulations, showing the powder has good flow characteristics.

Angle of repose

In all formulations, the hausner ratio varies from 0.97 to 1.22, demonstrating the powder's favourable flow properties.

Table 4: Micromeritic properties of powder blend.

Formulation Code	Bulk density	Tapped density	Compressibility Index	Hausner's ratio	Angle of repose
F1	0.52	0.54	15.32	0.98	24.05
F2	0.54	0.55	13.07	0.97	23.26
F3	0.55	0.56	14.42	0.98	23.05
F4	0.56	0.57	15.17	1.04	24.36
F5	0.55	0.54	17.68	1.15	22.04
F6	0.56	0.55	14.34	1.17	23.15
F7	0.54	0.56	15.93	0.98	22.05
F8	0.53	0.55	16.20	1.19	23.04
F9	0.54	0.56	15.12	1.22	21.06

Post compression evaluation parameters of quetiapine floating tablets**Appearance**

Visual inspection of the tablets revealed no signs of capping, chipping, or lamination.

Physical characteristics: The weight variation, thickness, hardness, friability, and drug content of quetiapine floating tablets (F1 to F9), as well as other physical properties, were assessed, and the formulations' findings (F1 to F9) were found to be within the bounds prescribed in official books.

a) Thickness

Specifications for thickness and diameter can be established for each product separately. Too much variance in tablet thickness might cause packaging issues as well as concerns with consumer acceptance. Within each formulation, the thickness of the tablets did not differ noticeably, showing that the powders behaved uniformly throughout the compression process.

All tablet formulations were determined to have a thickness that fell between 2.1 and 2.5 mm.

b) Hardness

A difference in tablet density and porosity will result in a difference in tablet hardness. The hardness of tablets was discovered to be between 3.4 and 3.6 Kg/cm².

c) Percentage friability

All formulations' percentage friability was discovered to be between 0.52% and 0.57%. This suggests that the produced tablets have good handling characteristics.

d) Weight variation

The tablet weighs 300 milligrams on average. The maximum percentage variance allowed by the pharmacopoeia is 5%. All of the tablets had weights between 297 mg and 305 mg.

e) Drug content

The drug concentration of all floating tablet formulations has been consistent and has ranged from 97.76 to 99.41%, which is within the allowed range. The outcomes were displayed in table no. 8.3.

Table 5: Evaluations of physical parameters of tablets.

Formulation Code	Weight variation (mg)	Thickness (mm)	Hardness (Kg/cm ²)	Friability (%)	Drug content (%)	Floating lag time (sec)	Floating buoyancy time (hrs)
F1	301	2.3	3.4	0.52	97.76	101	11
F2	305	2.1	3.5	0.55	98.37	98	12
F3	300	2.3	3.4	0.53	99.02	106	>12
F4	298	2.2	3.6	0.54	98.62	107	12
F5	304	2.5	3.5	0.56	99.05	103	11
F6	299	2.4	3.6	0.57	98.10	99	12
F7	304	2.5	3.4	0.54	98.62	104	12
F8	299	2.2	3.4	0.56	99.41	108	>12
F9	297	2.4	3.5	0.55	98.76	110	12

f) In-vitro buoyancy studies

An effervescent method was chosen to produce in vitro buoyancy. To create gas, sodium bicarbonate was used. The interaction between the acidic liquid and sodium bicarbonate caused CO₂ to be produced as the dissolving medium (0.1N HCl) absorbed into the tablet matrix. The polymer protected and enclosed the produced gas, reducing the density of the tablet. The tablet became buoyant when its density decreased below 1. To prevent the dose form from passing into the small intestine with meals, the system must float within a few minutes of

coming into touch with stomach fluid. All of the formulations (F1 through F9) displayed a floating lag of about 110 seconds. The outcomes were displayed in table number 5

In-vitro drug release studies

The in-vitro drug release statistics of all formulations are presented in the table. The in-vitro dissolving experiments of floating tablets of quetiapine were carried out in simulated gastric fluid 0.1N HCl for 12 hours.

Table 6: Drug release data of Quetiapine floating matrix tablets.

Time(Hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	6.21	7.35	6.35	9.10	8.14	9.34	8.12	7.14	9.13
1	17.93	14.58	14.23	16.38	14.05	17.12	15.73	13.05	17.56
2	24.40	22.04	21.18	29.34	22.92	25.39	22.13	20.34	24.49
3	30.93	29.73	29.05	35.10	29.17	32.73	31.11	27.13	30.42
4	36.07	37.62	35.21	41.21	37.63	38.16	37.86	35.61	37.76
5	42.56	45.04	41.27	47.17	48.11	45.54	44.32	46.58	46.53
6	49.84	57.68	49.13	53.34	55.48	52.76	52.86	54.92	55.10
7	57.92	64.12	57.87	60.87	61.34	57.42	59.93	60.73	61.21
8	63.34	72.34	65.24	65.63	67.18	64.73	66.54	66.13	68.09
9	69.06	78.42	71.12	72.24	73.13	71.58	72.81	78.19	75.12
10	73.12	82.13	77.34	80.13	80.21	77.26	77.52	87.76	81.32
11	80.57	89.16	82.12	86.20	85.24	84.24	82.12	92.13	87.13
12	87.23	93.21	91.32	92.41	91.32	91.83	90.34	97.81	93.16

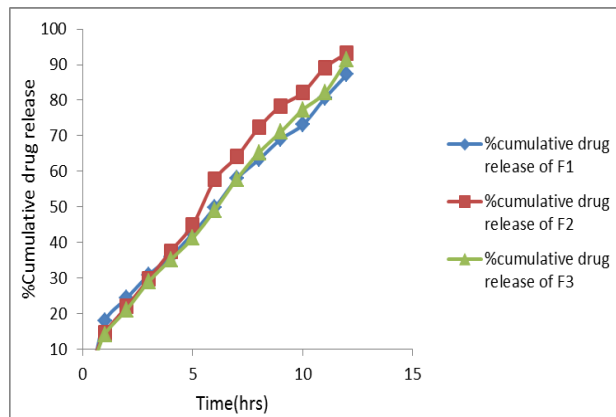


Fig. 2: % drug release of formulation (F1-F3).

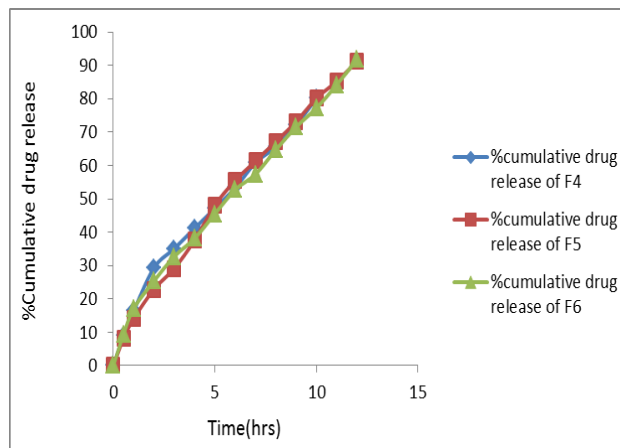


Fig. 3: % drug release of formulation (F4-F6).

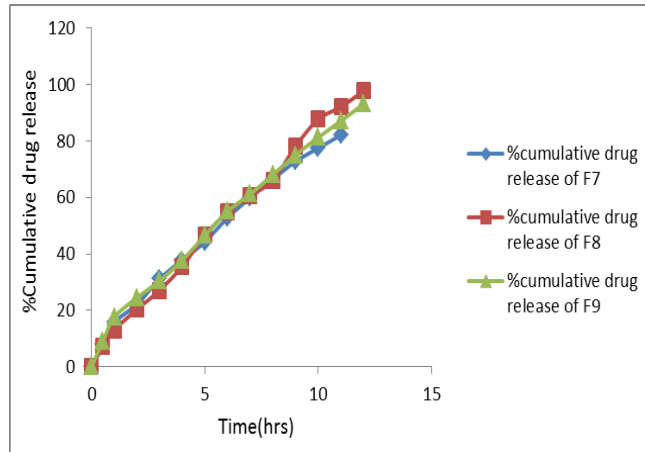


Fig. 4: % drug release of formulation (F7-F9).

Because it achieved the specified drug release profile with a 97.81% accuracy, formulation F8 was regarded as

the best one. Table No. 6 and Figure Nos. 2, 3, and illustrate the results, accordingly.

Release kinetics

Table 7: Release kinetics data for optimized formulation.

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	Qt1/3	Q01/3-qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
7.14	0.5	0.707	0.854	-0.301	1.968	14.280	0.1401	-1.146	92.86	4.642	4.528	0.113
13.05	1	1.000	1.116	0.000	1.939	13.050	0.0766	-0.884	86.95	4.642	4.430	0.211
20.34	2	1.414	1.308	0.301	1.901	10.170	0.0492	-0.692	79.66	4.642	4.303	0.339
27.13	3	1.732	1.433	0.477	1.863	9.043	0.0369	-0.567	72.87	4.642	4.177	0.465
35.61	4	2.000	1.552	0.602	1.809	8.903	0.0281	-0.448	64.39	4.642	4.008	0.633
46.58	5	2.236	1.668	0.699	1.728	9.316	0.0215	-0.332	53.42	4.642	3.766	0.875
54.92	6	2.449	1.740	0.778	1.654	9.153	0.0182	-0.260	45.08	4.642	3.559	1.083
60.73	7	2.646	1.783	0.845	1.594	8.676	0.0165	-0.217	39.27	4.642	3.399	1.243
66.13	8	2.828	1.820	0.903	1.530	8.266	0.0151	-0.180	33.87	4.642	3.235	1.406
78.19	9	3.000	1.893	0.954	1.339	8.688	0.0128	-0.107	21.81	4.642	2.794	1.848
87.76	10	3.162	1.943	1.000	1.088	8.776	0.0114	-0.057	12.24	4.642	2.305	2.337
92.13	11	3.317	1.964	1.041	0.896	8.375	0.0109	-0.036	7.87	4.642	1.989	2.652
97.81	12	3.464	1.990	1.079	0.340	8.151	0.0102	-0.010	2.19	4.642	1.299	3.343

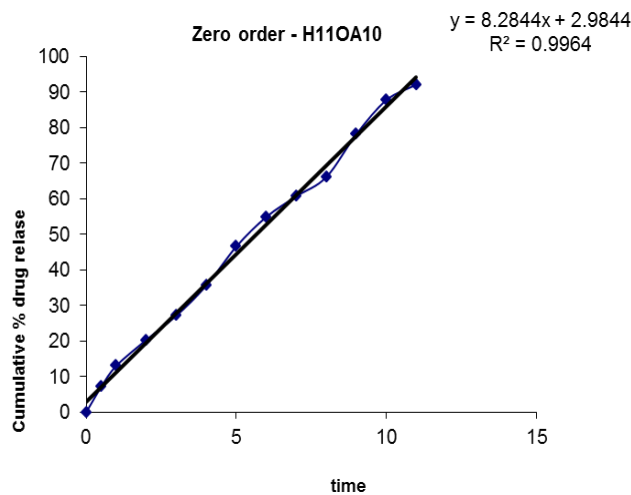


Fig. 5: Zero order release kinetics graph.

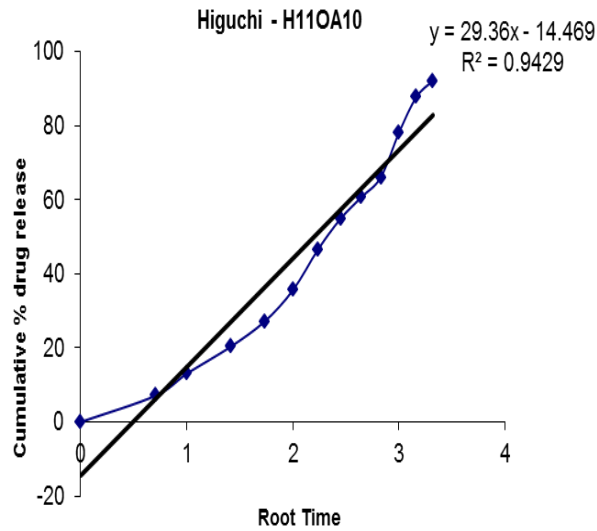


Fig. 6: Higuchi release kinetics graph.

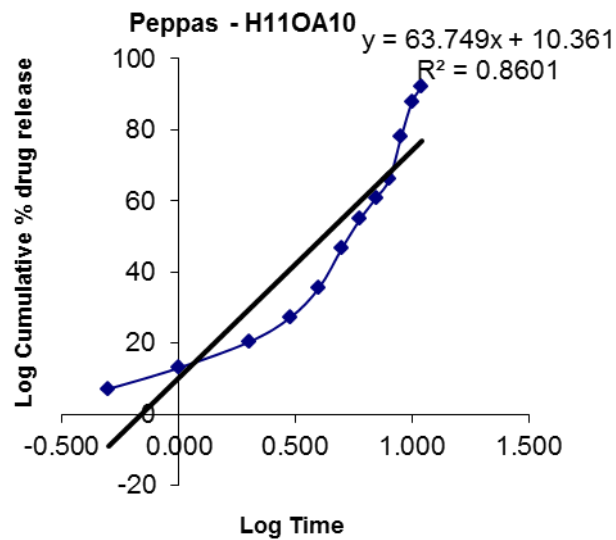


Fig. 7: Kars mayerpeppas graph.

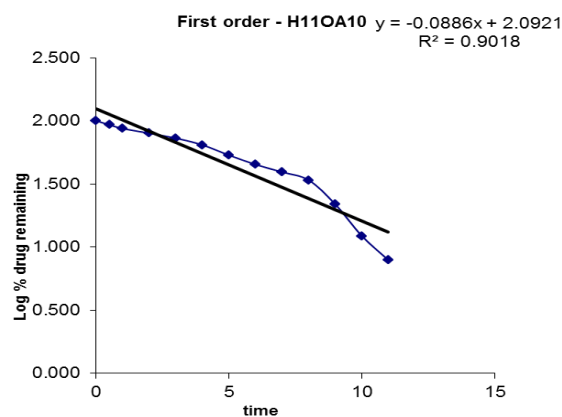


Fig. 8: First order release kinetics graph.

CONCLUSION

The preparation of gastro-retentive floating tablets containing quetiapine fumarate is the goal of the current effort. Different amounts of retardation polymers were applied together with the gas-generating agent accural at

various concentrations. As retarding polymers, carbopol 971, carbopol L934P, and carbopol HPMCK100M were employed. The formulation blend's physicochemical properties were assessed, and all the parameters were found to be within acceptable bounds. For various quality

control parameters, the formulations F1–F9 were developed and assessed. All of the formulas passed the tests, and the outcomes were acceptable. According to the dissolution results, formulation F8 was the best, with a maximum percent drug release of 97.81% and a floating time of 12 hours.

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