Formulation Development and Evaluation of Orodispersible Tablets of Quetiapine Fumarate by Sublimation Method

Phulzalke S.B.,B A Kate, Bagade M. Y., Shete RV
Rajgad Dnyanpeeth's College of Pharmacy, Bhor, Pune.4122062.

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ABSTRACT :
The objective of present study was to formulate directly compressible orodispersible tablets of quetiapine fumarate by sublimation method with a view to enhance patient compliance. A full 32 factorial design was used to investigate the effect of two variables viz., concentration of Indion 414 and camphor. Indion 414 (3-5 % w/w) was used as superdisintegrant and camphor (5-15 % w/w) as subliming agent. The tablets were evaluated for thickness, weight variation, hardness, friability, content uniformity, wetting time, porosity, in vitro disintegration time and in vitro drug release. In vitro dissolution profile revealed faster and maximum drug from formulation F3. SEM study show formation of pores on tablet surface after sublimation of the sublimating agent, thus providing a sufficiently porous structure. This permitted the selection of a batch of tablets with desired disintegration time and improved dissolution rate after oral administration. The F3 batch containing the Indion 414 (5%) and Camphor (5%) w/w of total formulation weight had shown good the disintegration time of 18.66 seconds and with improved dissolution rate and desirable friability. Further studies will be required to evaluate the performance of dosage form in vivo and In Vitro In vivo Correlation.

Key words: Orodispersible tablet, factorial design, Indion 414, sublimation, quetiapine fumarate.

INTRODUCTION:

A basic tenet of pharmaceutical formulation science is that the dosage form exists to optimize the delivery of a pharmaceutical active to its site of action in the most effective and safe manner.[1] Solid oral dosage forms offers noncompliance to patient owing to problems such as dysphagia, risk of choking, and hand tremors. Solid dosage forms also present substantial difficulties in patients such as children, mentally challenged, uncooperative and patient on reduced fluid diet[2].To fulfill these medical needs, pharmaceutical technologists have developed a novel oral dosage form known as ODTs which disintegrate rapidly in saliva, usually within a matter of seconds, without the need to take it water. Drug dissolution and absorption, as well as onset of clinical effect and drug bioavailability, may be significantly greater than those as compared with conventional dosage forms [3-5].

ODTs are also called as orodispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and rapid melts. However, of all the above terms, United States pharmacopoeia (USP) approved these dosage forms as ODTs.

Quetiapine fumarate is atypical antipsychotic drug, used in the treatment of schizophrenia and bipolar disorders[6]. Quetiapine Fumarate bioavailability is 9%. Half-life of drug is

Approximately 6 hrs. It is preferable to administer in the form of fast disintegrating tablets used for depressive episodes, acute manic episodes associated with bipolar I disorder at [7-9].

In certain diseases or disorder such as psychotherapy, hypertension, angina, myocardial disorder therapy, taking fast pharmacological response is an important criteria.The patients would be benefitted by proposed drug delivery with sudden episode of psychotic attack and need to calm down quickly.

Hence the present study was undertaken to develop orodispersible tablets of quetiapine fumarate with shorter disintegration time, greater drug release and lesser friability with a prospect of assisting various patients who have difficulty in swallowing conventional dosage forms.

Material and methods

Quetiapine fumarate was obtained as gift sample from Alkem Pvt. Ltd, Mumbai, India. Sucralose, camphor, magnesium stearate, and talc were procured as gift samples from Research Lab Fine Chem Industries, Mumbai. Indion 414 was received from Ion Exchange India Ltd, Gujarat. All other chemicals were of analytical reagent grade.

***Corresponding author:**
Phulzalke S.B
Rajgad Dnyanpeeth's College of Pharmacy, Bhor, Pune.4122062.

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Preparation of orodispersible tablets by sublimation method

All of the formulation components other than lubricant and glidant were accurately weighed, passed through 60-mesh sieve and mixed in vertical blendor for 30 min. Talc and magnesium stearate were passed through 80-mesh sieve, mixed with above blend for 10 min and resultant blend was directly compressed into tablets. The amount of all tablet components other than superdisintegrants and Perlitol SD 200 were kept constant. Round concave tablets of 100 mg in weight and 7 mm diameter were prepared using Cadmach 13 station single sided rotary tablet press. Table 1 outlines the compositions of various ODT formulations studied. Compressed tablets were subjected to the sublimation process in hot air oven
at 50° for 6 h[10].

Table1: 32 factorial design formulations

Ingredient (mg)	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Quetiapine Fumarate	25	25	25	25	25	25	25	25	25
Indion-414	3	4	5	3	4	5	3	4	5
Camphor	5	5	5	10	10	10	15	15	15
Sucralose	2	2	2	2	2	2	2	2	2
Magnesium Stearate	1	1	1	1	1	1	1	1	1
Talc	1	1	1	1	1	1	1	1	1
Pearlitol SD-200	63	62	61	58	57	56	53	52	51
Total weight	100	100	100	100	100	100	100	100	100

Evaluation of precompression parameters of orodispersible tablets:

Prior to compression, powder blends were evaluated for flow and compressibility parameters. Flow properties of powder were determined by angle of repose and compressibility by Carr's index and Hausner ratio[11,12].

Evaluation of post compression parameters:

Thickness and weight variation:

The thickness of the tablets was measured using a digital Vernier caliper. Five tablets of each formulation were picked randomly and thickness of each of these tablets was measured.

Twenty tablets were selected at random and average weight was determined using an electronic balance (Shimadzu). Tablets were weighed individually and compared with average weight[13].

Hardness and friability:

Five tablets were randomly selected from each batch and hardness of tablets was determined by using Monsanto hardness tester. The mean values and standard deviation for each batch were calculated.

The friability of tablets was measured using USP type Roche friabilator. Preweighed tablets (equivalent to 6.5 g) were placed in plastic chambered friabilator attached to motor revolving at a speed of 25 rpm for 4 min. The tablets were then dedusted, reweighed, and percent weight loss was calculated using the formula, % friability=((initial weight–final weight)/initial weight)×100.

Drug content:

Twenty tablets were weighed and powdered. Powder equivalent to a single dose of quetiapine was weighed and assayed for drug content at 248 nm using a UV/Vis double beam spectrophotometer (Jasco V-530). The UV method was validated according to ICH guidelines (Q2 R1).

***In vitro* disintegration time:**

The digital tablet disintegration test apparatus (Veego) was used to determine *in vitro* disintegration time (DT) using distilled water at 37±2°. The time (s) taken by tablet for complete disintegration with no residue remaining in apparatus was recorded as mean±SD[14].

***In vitro* drug release study:**

The drug release studies were performed using the USP dissolution test apparatus (VDA-6DR USP Stds.,Veego) employing paddle method. The dissolution test was performed using 900 ml of 0.1 N hydrochloric acid at 37±0.5° and paddle speed of 50 rpm. Samples (5 ml) were collected at predetermined time intervals (1 min) and replaced with equal volume of fresh medium. The study was continued for 10 min, samples were then filtered through 0.45 µm membrane filter[15] and analyzed at 248 nm using UV/Vis spectrophotometer.

Wetting time:

Six circular tissue papers of 10 cm diameter were placed in a Petri dish and 10 ml of water containing amaranth dye was added to it to identify complete wetting of tablet surface. A tablet was carefully placed on the surface of tissue paper in Petri dish at ambient temperature. The time taken by water to reach upper surface of the tablet and to completely wet the tablet was noted as wetting time. The study was performed in triplicate and time was recorded using stopwatch.

Measurement of tablet porosity:

Porosity of the tablets was calculated from the weight of the tablet (W), ablet volume (V), and true density of powder (ρ) using following Eqn[18], %porosity=((1–weight of Tablet, W)/ volume V)×density (ρ). The true density of powder was determined by a pycnometer.

Drug-excipient compatibility study:

Preliminary compatibility studies were performed in closed vial using hot air oven and autoclave. The physical mixture (quetiapine+Indion 414, quetiapine+camphor) were prepared in 1:1 ratio by

SEM analysis

The surface morphology of optimized formulation before and after sublimation of camphor was studied using (GEOL Ltd. Japan-JSM-6360).The tablet surface was sputter coated for 10 minutes with gold by using fine coat ion sputter and examined under SEM.

***In vitro* dissolution Test**

Dissolution profiles of Quetiapine Fumarate tablets were determined using the USP Method II with pad-

dle speed at 50 rpm. Dissolution was performed in 900 ml 0.1N Hydrochloric acid maintained at 37 ± 0.5°C. 5 ml of samples were withdrawn at specified time intervals. The volume of dissolution fluid was adjusted to 900 ml, by replacing each 5 ml aliquot withdrawn with 5 ml of 0.1N Hydrochloric acid, pre-warmed at 37±0.5°C. Samples were withdrawn and analyzed at 248nm, using UV-Visible double beam spectrophotometer (Jasco-V -530). The data presented is the average of 3 individual determinations.

Stability Study

Stability studies were carried out according to ICH guidelines. Formulation F3(Optimized batch) was packed in marketed packs (that is aluminum foils) and kept for stability in triplicate and formula for stability batches were given below. Studies were carried out at 300 C/65%RH, 400C/75% RH, and at room temperature for a 30 days and it was evaluated for In vitro dissolution and disintegration time. All three stability batches were kept as per ICH conditions.

Preformulation Study

Organoleptic properties

Quetiapine Fumarate was evaluated for its organoleptic properties such as odour, colour, and taste, and it was found that the drug is odourless, tasteless, and having off white colour.

Solubility study

Solubility studies were carried out in three different Medias 0.1N Hydrochloric acid phosphate buffer of pH 6.8 and water. All Medias have shown different solubility as shown in Table 18. The solubility was found maximum in 0.1N Hydrochloric acid as compared to phosphate buffer of pH 6.8 and water. As saturation solubility was found maximum in 0.1N Hydrochloric acid, the dissolution media selected was 0.1N Hydrochloric acid.

Table 2 : Solubility study in different medias

Sr no.	Media	Solubility (mg/ml)
1	0.1 M HCl	161.26
2	Phosphate buffer pH 6.8	8.6
3	Water	1.25

Characterization of API and excipients

For each preliminary batch, blends of API and excipients were prepared and evaluated for various parameters as explained earlier.

The flow properties of each API and Excipients are shown in Table 3. The results indicated that the API has poor flow properties but formulation excipients have excellent flow properties.

Table 3: Flow properties of API and excipients

Parameters	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Carr's Index (%)	Angle of Repose	Hausner ratio	Conclusion
Quetiapine Fumarate	0.317	0.636	26.49	53.06°	1.39	Poor flow
Pearlitol SD 200	0.70	0.78	9	15.64°	1.1	Excellent flow
Indion 414	0.632	0.843	21.6	35.45	1.22	Passable

Drug and excipient compatibility study

The results of drug and excipient compatibility study are shown in Table 4. From the results it was found that the colour, odour and assay of drug and excipients were not changed, hence they are compatible with each other.

Table 4 : Compatibility study

Parameters	Instrument	Time	Temperature	Appearance	Result
QF + Kyron T 314	Hot air oven	1 month	40°C	Colour, Odour & Assay	No change
QF + Indion 414					
QF + Camphor					
Complete formulation					
QF + Kyron T 314	Autoclave	15min	121°C at 15 lb	Colour, Odour & Assay	No change
QF + Indion 414					
QF + Camphor					
Complete formulation					

Differential scanning calorometric analysis

The sharp endothermic peak of Quetiapine Fumarate was observed at 174.86°C with onset at 167.25°C. Sharp endothermic peak indicates the purity of drug sample shown in figure 3.

The DSC thermograph of Quetiapine Fumarate with Indion 414 and Camphor was recorded in order to study the drug excipient compatibility. Study also shows the sharp peak at 176.99°C and 177.16°C indicating compatibility of drug with

Indion 414 and Camphor respectively and shown in figure 4 and figure 5.

The DSC thermograph of formulation batch recorded in order to study the drug excipient compatibility. Study also shows the sharp peak at 178.87°C hence indicating compatibility of drug with all excipients. shown in figure 1.

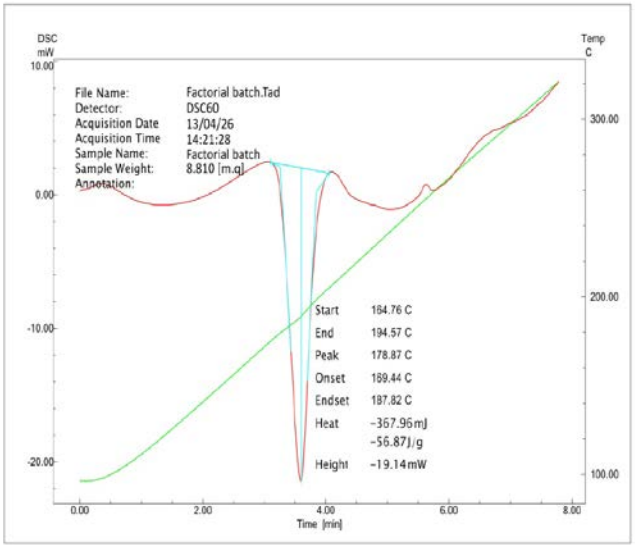

Figure 1: DSC Thermograph of factorial batch F3

IR spectroscopy analysis

The IR structure of Quetiapine Fumarate complies with the chemical structure 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]ethanol Fumarate. Various groups present are given in Table 21. From the spectra it can be seen that the –NH peak, -COOH broad band, -C-O-C- stretching at 3300.82/cm, 2889.00/cm, 1060.98/cm respectively does not changed with the addition of Indion 414 and camphor therefore excipient compatibility was seen.

Table 5 : IR Interpretation

Absorption peaks	Attributed to
3300.82	-NH stretching
2889.00	-COOH stretching
1060.98	-C-O-C- ether stretching

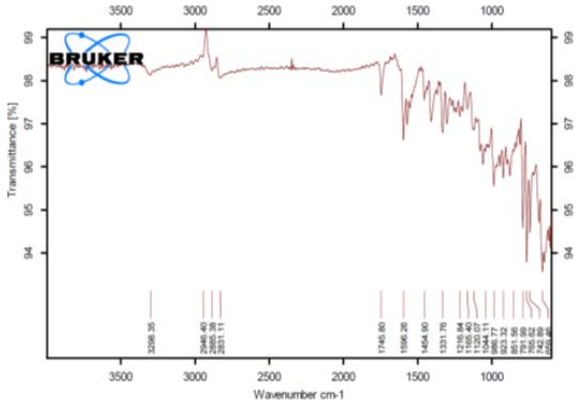

Figure 2 : IR spectra of Quetiapine Fumarate + camphor

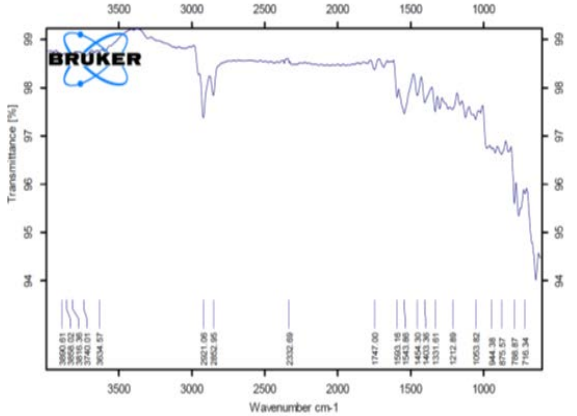

Figure 3 : IR spectra of formulation batch F3

From the above interpretation it is found that there is no major shifting in the frequencies of above said functional groups. Hence above result conclude that no drug and excipients interaction was found.

Analytical Method Validation

The analytical method was validated according to ICH giidlines for linearity and range, intraday and interday precision, accuracy, DL (Detection Limit) and QL (Quantitation Limit) and results are listed in Table 5.

Table 5: Method validation

Sr no.	Parameter	Result
1.	Linearity and range	10-30 µg/ml
2.	Accuracy	100.679%
3.	Intraday precision	0.722%RSD
4.	Interday precision	1.40% RSD
5.	DL	0.17069 g/ml
6.	QL	1.0901 µg/ml

Formulation and Development

In present research work Pearlitol SD 200 was used as the diluent due to its negative heat of solution and property to give pleasant mouth feel and also have excellent flow property.

Flow properties of formulation batches

Factorial batches were evaluated for their flow properties. The results are presented in Table 6 and it was found that all factorial batches showed good flow properties.

Table 6 : Evaluation Flow Property of formulation Batches

Formulation Code	Bulk Density (gm/cm^3)	Tapped Density (gm/cm^3)	Carr's Index (%)	Hausner Ratio	Angle of Repose (θ)	Flow
F1	0.795	0.84	18.36	1.19	29.24	Good
F2	0.816	0.85	18.51	1.15	29.68	Good
F3	0.743	0.91	17.36	1.31	26.56	Good
F4	0.82	0.86	15.86	1.21	27.92	Good
F5	0.73	0.96	13.20	1.18	29.24	Good
F6	0.71	0.88	11.85	1.22	26.54	Good
F7	0.72	0.84	12	1.10	27.92	Good
F8	0.752	0.90	11.62	1.19	29.68	Good
F9	0.86	0.95	13.40	1.14	27.02	Good

Evaluation of formulation batches

All the tablet formulations were subjected for organoleptic, physical and chemical evaluations as shape, thickness, hardness, friability, weight variation, *In vitro* disintegration time, wetting time, drug content and *In vitro* dissolution studies.

Appearance

The size and shape of the tablets can also affect the disintegration time and subsequent dissolution profile. In general, a smaller tablet in terms of mass has a faster disintegration time than larger tablets, all other factors being equal. Similarly, a tablets shape with more surface area generally has faster disintegration time than a tablets shape having less surface area, all other factors being equal. Randomly picked tablets from each formulation batch examined for shape and in presence of light for colour. Tablets showed curved shape and white colour.

Weight variation test

The percentage weight variation for all the formulations are tabulated in Table 30. All the tablets passed weight variation test as the % weight variation was within the pharmacopoeial limits of 130 ±10%. The weight of all the tablets was found to be uniform. Uniform weight due to uniform die fill with acceptable variation as per USP standards were obtained since blend of material was free-flowing. Weight Variation Before and After Sublimation shown in Table 7.

Table 7 : Weight variation before and after sublimation

Formulation code	Camphor(mg)	Sublimation	
		Before(mg± SD)	After(mg ±SD)
F1	5	99.8±0.83	95.857±0.85
F2	5	99.2±0.83	96.12±0.60
F3	5	100.2±0.83	95.983±0.48
F4	10	101.8±0.44	92.137±0.82
F5	10	100.8±0.44	90.96±0.20
F6	10	101±0.70	90.967±0.522
F7	15	99.6±0.89	86.217±0.55
F8	15	99.4±0.89	85.26±0.55
F9	15	100.4±0.89	86.513±0.30

Hardness

Tablet crushing strength, the critical parameter was controlled as the resistance of tablets to capping, abrasion or breakage under conditions of storage, transportation and handling before usage depends on its hardness. Hence, hardness for all Trial batches and Factorial batches were between 3-4 kg/cm^2. The results are shown in Table 30. These results are observed due to constant tablet press setting across all batches design irrespective of weight variation.

Thickness

The thickness of the tablets was measured by using Digital Vernier Caliper by picking the tablets randomly. The values are shown in Table 30. The values were almost uniform in all formulations. Thickness for all formulation batches was found between 2.62 – 2.66 mm due to constant tablet press setting across all batches design irrespective of weight variation with constant diameter of 7mm.

Friability

To achieve percent friability within limits for a fast dissolving tablet was challenge to the formulator since all methods of manufacturing of Fast dissolving tablets was responsible for increasing the percentage friability values. The percentage friability values for all formulation batches were found between 0.33 - 1.11%, due to constant tablet press setting across all batches of design irrespective of weight variation. The results of friability are given in Table 30.

Drug content

Drug content for all formulation batches was found to be in the range of 98.26% to 100.96%. The results are shown in Table 30. The results indicated that in all the formulations the drug content was uniform.

Wetting time

Wetting time for all formulation batches showed wide variations in the range in between 16.00 and 30.00 second. The result of wetting time are shown in Table 30.This wide variation range was observed due to developmental changes in formulation to attain preliminary objectives.

Rapid disintegration of prepared tablets may be attributed to increase in the ability of water to penetrate into tablet due to high porosity achieved by the increase in number of pores after sublimation of camphor. The study indicate that porous cavities were formed in tablets due to sublimation of camphor and increase in concentration of camphor decreased the wetting time significantly.

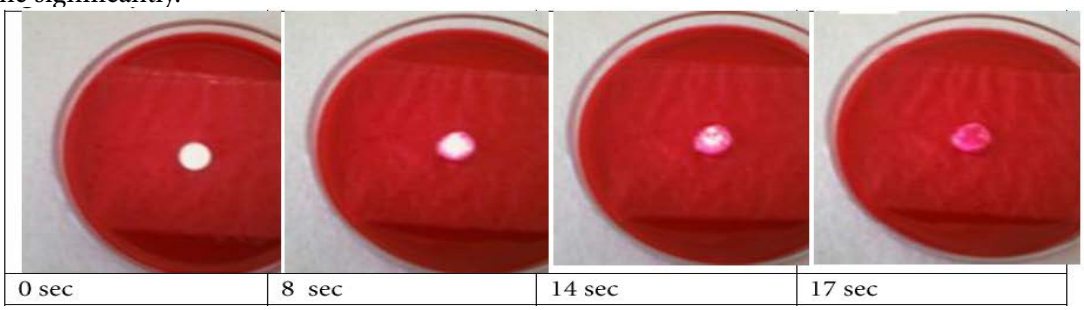

Figure 4 : Wetting time study of F3 batch

In vitro disintegration time

All tablets disintegrated rapidly without disc in test especially when used at optimum concentrations of selected superdisintegrants. The results are shown in Fig 5. It was observed that with 3% concentration of Indion 414, disintegration time was increased that might be due to lower concentration of superdisintegrant which may not be sufficient for swelling of tablet, while with 5% Indion 414 disintegration time was decreased due to optimum swelling of tablet required for effective disintegration. At this particular concentration DT was decreased considerably to 18 seconds only. To shorten disintegration time in the oral cavity, the addition of the disintegrating agent having a property of quick water uptake in the formulation would be preferable. Camphor exhibits very good disintegrant property when present in as low as 5-15%

concentration and after sublimation pores are formed. It functions by allowing water to enter the tablet matrix by means of capillary pores. Perlitol SD-200 also exhibits very good disintegrant property when present in low optimum concentrations. Major mechanism of disintegration of Pearlitol was due to quicker water uptake and less time for wetting. When higher percentage of Pearlitol SD-200 and Camphor was used, tablets of high porosity were expected. *In vitro* disintegration time for factorial batch F3 containing 5% Indion 414 and 5% Camphor gives best results among the factorial batches.

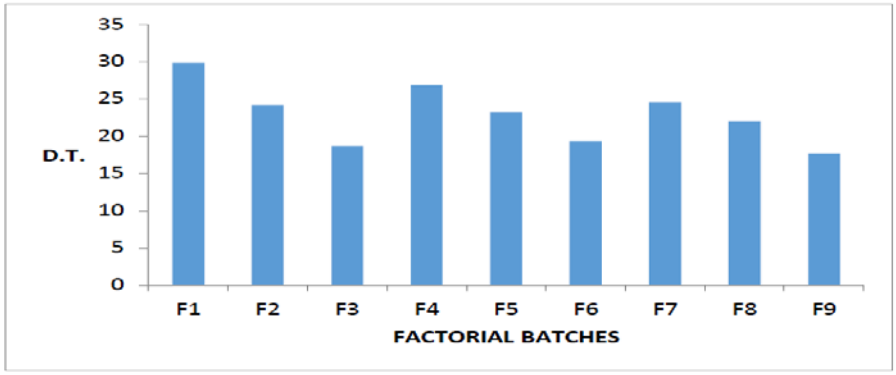

Figure 5 : DT of factorial batches

In vitro dissolution study

As discussed above, differences in the particle size generated in the disintegrated tablets could affect drug dissolution. Since breaking the tablet into finer fragments may promote drug dissolution by providing larger total surface areas for drug dissolution to take place. Percent Drug released at 60 seconds ($\%DR_{60sec}$) for factorial batches that is F1 to F9 showed wide variation in the range of 51.32 to 75.38%.The Factorial batches F1, F2, F3 contain 5% of Camphor and 3%, 4%, 5% Indion 414 respectively. The dissolution behaviour of F1, F2, F3 at 60 seconds was found to be 51.32%, 62.46%,72.42% The results are shown in Figure 6.

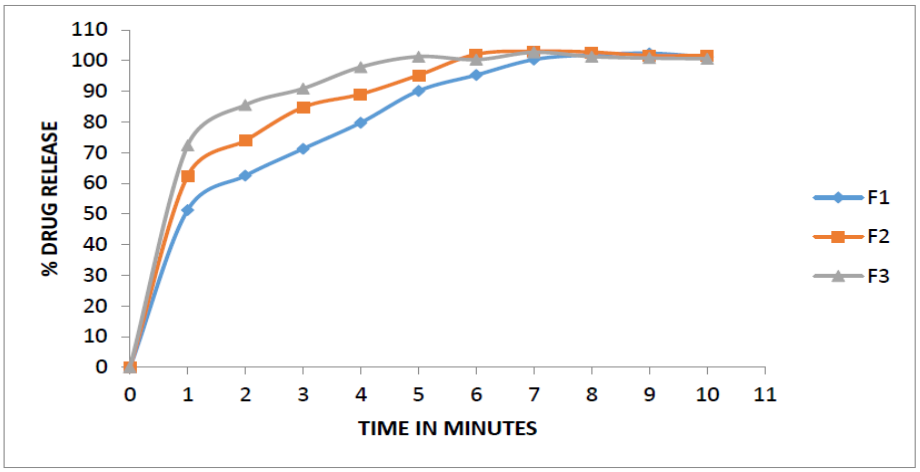

Figure 6 : *In vitro* dissolution profile for F1, F2, F3 batches

F4, F5, F6 contains 10% Camphor and 3%,4%,5% Indion 414 respectively. The release was found to be 55.88%, 68.83%,74.64%. The results are shown in Figure 7.

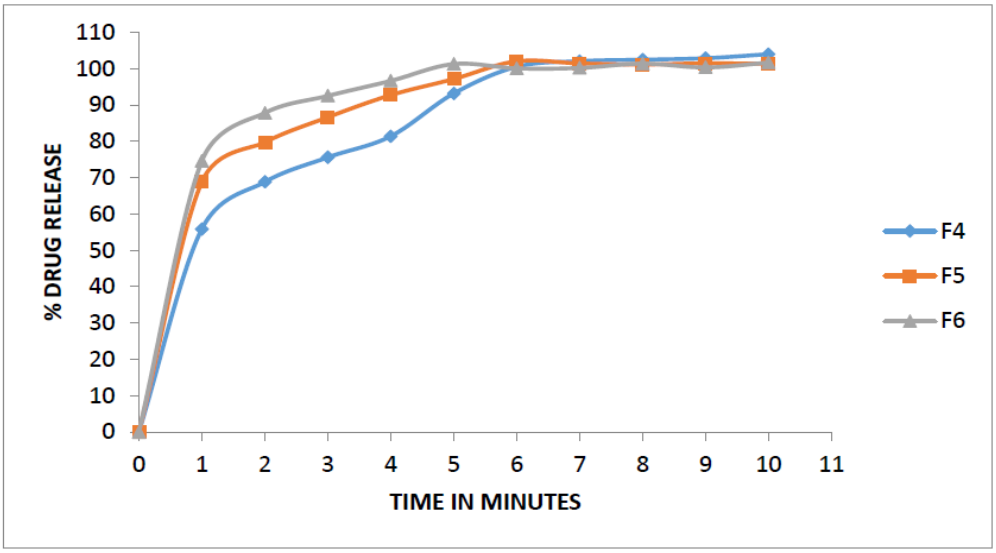

Figure 7: *In vitro* dissolution profile for F4, F5, F6 batches

Finally at F7, F8, F9 the release was found to be 55.39, 75.13, 75.38%. The results were shown in Figure 8. All the 9 batches were comprised of 5, 10 and 15% of Camphor with each level of Indion 414 mentioned above. These batches showed wide variation in their $\%DR_{60sec}$ because of change in not only type but also amount of proportion of superdisintegrants taken for study. The results of $\%DR_{60sec}$ were shown in Figure 20.Hence it was evident that selected superdisintegrant and camphor for study played vital role in dissolution behaviour. The better $\%DR_{60sec}$ was found with F3 batch containing 5% Indion 414 and 5% Camphor.

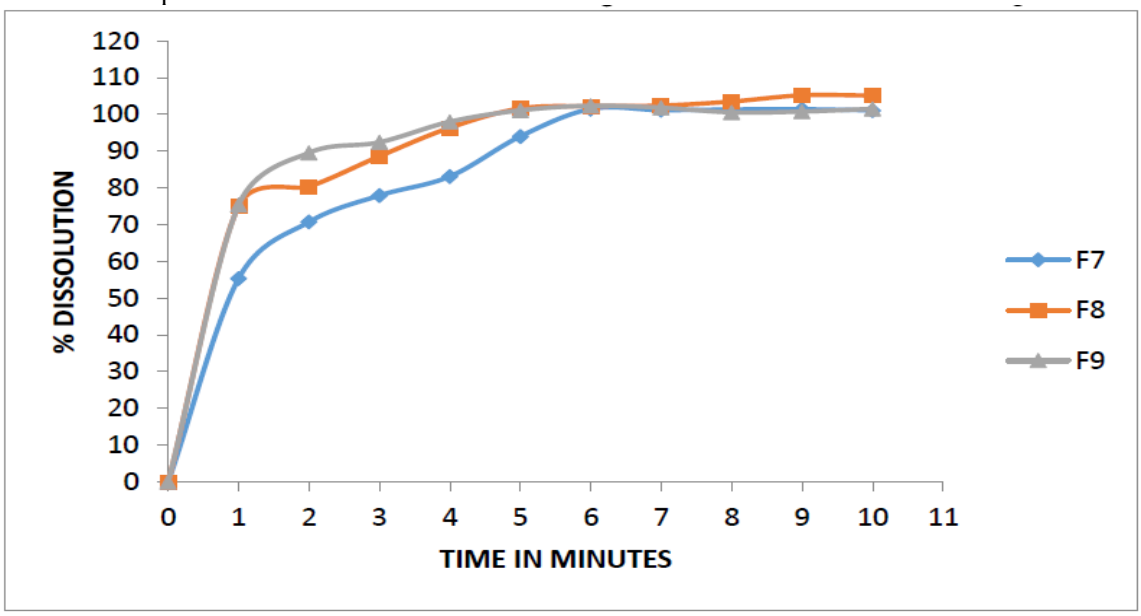

Figure 8 : *In vitro* dissolution profile for F7, F8, F9 batchs

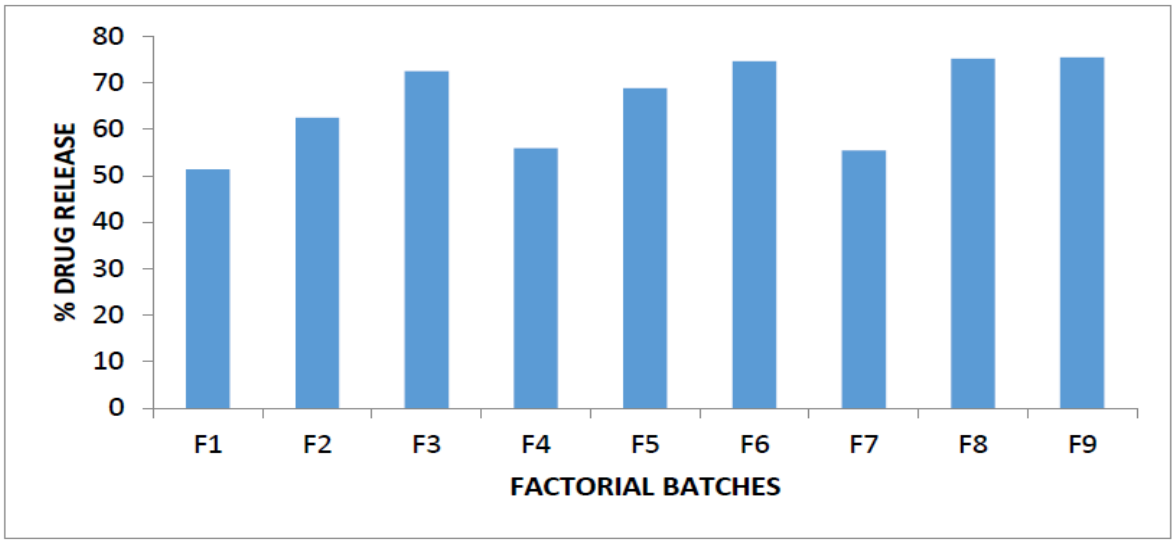

Figure 9: % Drug Release in 60 sec

The aim of study was to assess in vitro dissolution behaviour of developed formulations. The drug released at 60 sec was considered, the result are presented in Table 29 and indicates that F1 formulation showed minimum DR at 60 second where as maximum drug was released by F9 formulation. These variations may be attributed to different concentration of camphor and superdisintegrant used. However, F3 batch showed comparable DR to F9 formulation with minimum concentration of sublimating agent in the formulation. Also evaluation parameters for F3 batch were optimum viz. hardness, thickness, friability, wetting time, DT. Hence F3 batch was optimized.

Table 8 : Evaluation of formulation batches

Batch code	Hardness (kg/cm^2)	Thickness (mg ±S.D)	Drug content (%±S.D)	In-vitro DT (Sec±S.D)	Wetting time (Sec±S.D)	Friability (%±S.D)	% Drug release in 1 min. (%±S.D)	%Porosity (%±S.D)
F1	3-3.5	2.6±0.20	99.94±0.37	29.08±0.98	29.16±0.98	0.383±0.12	51.32±0.08	12.76±0.96
F2	3-3.5	2.66±0.35	98.31±.14	24.16±0.98	23.33±1.50	0.334±0.10	62.46±0.11	13.48±1.49
F3	**3-3.5**	**2.63±0.30**	**100.96±0.73**	**18.66±1.03**	**16.66±1.21**	**0.367±0.10**	**72.42±0.26**	**14.64±1.65**
F4	3-3.5	2.66±0.20	98.83±0.11	26.83±1.47	23.83±1.32	0.726±0.17	55.88±0.6	23.71±0.97
F5	3-3.5	2.66±0.15	98.26±0.17	23.16±0.752	22.5±1.51	0.68±0.10	68.83±0.07	25.36±1.71
F6	3-3.5	2.63±0.32	99.15±0.13	19.33±1.03	16.8±1.60	0.60±0.15	74.64±0.05	27.69±1.07
F7	3-3.5	2.63±0.15	99.04±0.05	24.5±1.048	22.66±1.36	1.14±0.14	55.39±0.08	39.69±1.07
F8	3-3.5	2.6±0.20	98.85±0.03	22±0.89	19.16±1.16	1.13±0.16	75.13±0.56	40.91±0.81
F9	3-3.5	2.63±0.15	99.16±0.05	17.66±1.36	16.33±1.21	1.11±0.14	75.38±0.08	41.01±1.25

Porosity

Tablets exhibit % porosity in the range of 12.76 to 41.01 for camphor concentration in the range of 5 to 15 mg. Hence many porous structures are responsible for faster water uptake hence reduced wetting time; it also facilitates wicking action of Indion-414 bringing about faster disintegration. The results of Porosity are shown in Table 30.

Surface topography

The image show formulation of pores on tablet surface that may have extended into the matrix after sublimation of the sublimating agent, thus providing a sufficiently porous structure to facilitate rapid penetration of dispersion medium. This is evident from the magnified tablet surface images (Figure 10) of mouth dissolving tablet before and after sublimation.

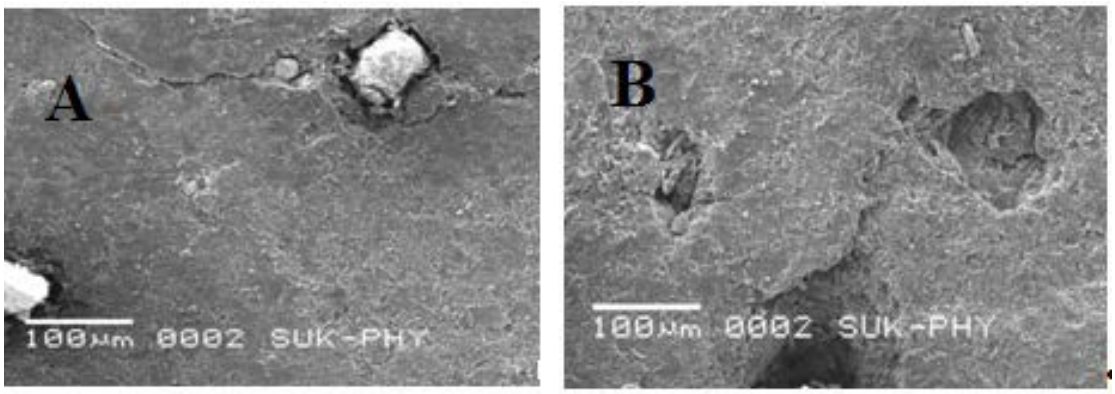

Figure 10 : SEM of optimized formulation F3 before sublimation (A) and after sublimation(B)

Comparison of optimized factorial batch with marketed preparation

Since in the market ODT preparation is not available for Quetiapine fumarate, therefore our formulation was compared with conventional marketed tablet formulation under the brand name 'Qutipin' The marketed formulation was evaluated for Disintegration time.

Disintegration time

The disintegration time of conventional marketed preparation (Qutipin) was found to be 266 sec and that of F3 batch was 18 sec. The results were shown in Figure 11.

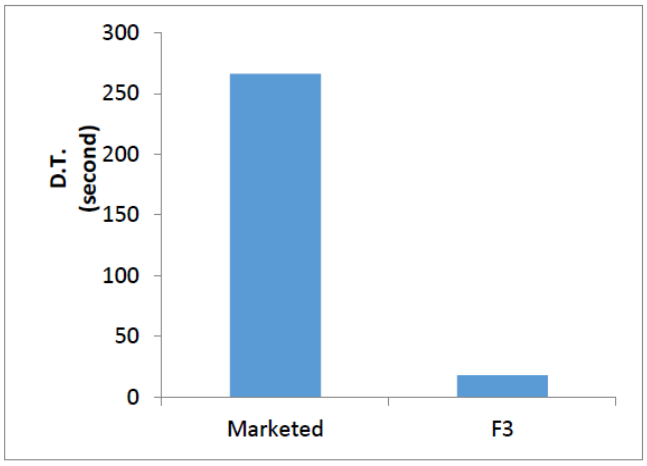

Figure 11 : Comparison of disintegration time of marketed conventional tablet and F3 formulation

Stability study

Stability study was conducted as per ICH guidelines. There was no significant change in colour and odour. There was no significant variation in *In vitro* disintegration time, dissolution time and wetting time profiles after one month stability study for optimized formulation at different temperature. The results are shown in Table 9

Table 9 : One month stability data at room temperature

Formulation Parameter	R.T	30^{0}C ± 2^{o}C /65% RH ± 5% R	40^{0}C ± 2^{o}C /75% RH ± 5% R
Colour	White	White	White
Odour	No	No	No
Hardness	3-3.5	3-3.5	3.5
Friability	0.367±0.10	0.394±0.12	0.417±0.14
Assay (%)	100.96±0.73	99.15±0.13	98.88±0.11

The directly compressible ODTs of quetiapine fumarate with shorter disintegration time, greater drug release and low friability (good mechanical strength) were obtained using Indion 414, camphor and other excipients at tested concentrations.

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