International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol.6, No.3, pp 1085-1095, July-Aug 2014

Formulation and Evaluation of Fast Dissolving Tablets of Flunarizine Hydrochloride by Sublimation method using Sodium Starch Glycolate as Superdisintegrant

Ronald Peter*[1], Shashank Nayak N[1], Shwetha S Kamath K[2], A. R. Shabaraya[2]

Department of Pharmaceutics, Srinivas College of Pharmacy, Valachil, Mangalore - 574143 Karnataka, India.

***Corres.author: ronaldthekkanath@gmail.com**
Tel.: +91 9497475313, +91 9916825572

Abstract: In the present work, Flunarizine hydrochloride, an anti-migraine drug has been formulated into fast dissolving tablets by sublimation method using camphor and menthol as sublimating agents and sodium starch glycolate as superdisintegrant. Concentrations of the sublimating agents were varied keeping the concentration of superdisintegrant fixed. The aim of the study was to prepare fast dissolving tablets with better drug releasing profile. The comparative evaluation of selected concentrations of sublimating agents on various physico-chemical properties of tablets was performed. Wetting time, water absorption ratio, *In-vitro* disintegration time, and drug release was dependent on the concentration of sublimating agents. The fast dissolving tablets were prepared with 0%-26.5% concentration of sublimating agents with optimum concentration of 4% of SSG. The blend was evaluated for angle of repose, bulk density, tapped density, compressibility index and hausner's ratio. The tablets were evaluated and compared for thickness, hardness, friability, weight variation, content uniformity, wetting time and water absorption ratio, *In-vitro* disintegration time, dissolution study and FTIR studies. The formulation F8 with 26.5% of menthol and 4% of SSG was found to be best with a better drug release of 99.92% in 5mins. We could conclude that, sublimating agent, menthol was better compared to camphor.
Keywords: Flunarizine hydrochloride, camphor, menthol, Sodium Starch Glycolate, *In-vitro* dispersion time, dissolution time.

Introduction

Swallowing a tablet is a major difficulty encountered in case of geriatric and pediatric patient this leads to poor patient compliance due to unpalatable taste of drug. To troubleshoot these problems a new dosage form known as fast-dissolving tablet, has been developed which rapidly disintegrate and dissolve in saliva. The conventional tablet seems to be most popular because of its ease of transportability and comparatively low manufacturing cost but poor patient compliance in case of pediatrics and geriatrics patients who experienced difficulties in swallowing, in response to this mouth dissolving drugs delivery system (MDDs) were developed as an alternative to tablet, capsules & syrups.[1] For conditions where treatments with FDT formulations are already available, there are studies showing that patients prefer these formulations to oral tablets. We can see that a fast dissolving pharmaceutical form could help to increase patient compliance, in view of its ease of administration, since they do not need to be taken with liquid like conventional formulations.[2]

Superdisintegrant are the agents added to tablet and some encapsulated formulations to promote the breakup of the tablet and capsule "slugs' into smaller fragments in an aqueous environment there by increasing

the available surface area and promoting a more rapid release of the drug substance. They promote moisture penetration and dispersion of the tablet matrix.[3] Superdisintegrant provides quick disintegration due to combined effect of swelling and water absorption by the formulation. Due to swelling of superdisintegrants, the wetted surface of the carrier increases, this promotes the wettability and dispersibility of the system, thus enhancing the disintegration and dissolution.[4]

The presence of a highly porous structure in the tablet matrix is the key factor for rapid disintegration of MDTs. Even though the conventional tablets contain highly water-soluble ingredients, they often fail to disintegrate rapidly because of low porosity. To improve the porosity, volatile substances such as camphor can be used in tableting process, which is later sublimated from the formed tablet.[5]

Flunarizine hydrochloride is a selective calcium channel blocker and coupled with its antihistaminic property it is claimed to be effective in prophylaxis of migraine. It is effective in migraine by reducing intracellular Ca^{2+} overload due to brain hypoxia and thus prevents the deleterious effects of cellular calcium overload. With a very long half-life, Flunarizine may be given once daily; and drowsiness, the main side effect, can be minimized by taking the daily dose in the evening.[6]

Sodium starch glycolate is widely used in oral pharmaceuticals as a disintegrant in capsule and tablet formulations. It is recommended to use in tablets prepared by either direct-compression or wet-granulation processes. The recommended concentration in a formulation is 2-8%, with the optimum concentration about 4% although in many cases 2% is sufficient. Disintegration occurs by rapid uptake of water followed by rapid and enormous swelling.[7]

In the present study an approach has been made to prepare and evaluate fast dissolving tablets of Flunarizine hydrochloride using various concentrations of sublimating agents such as camphor and menthol along with fixed concentration of SSG as superdisintegrant.

Materials and Methods

Materials:

Flunarizine hydrochloride was obtained as a gift sample from Novartis, Mumbai. SSG and Camphor was obtained from Yarrow chem Pvt ltd, Mumbai and Menthol was obtained from Himedia Pvt ltd, Mumbai. All other chemicals used were of analytical grade.

Methods:

Excipients Compatibility Study:

Drug: Excipients compatibility study was carried out for any interference of drug and excipients used for the formulation of mouth dissolving tablet of Flunarizine HCl. The interference study was carried out using FTIR. The infrared absorption spectra of pure drug, physical mixture of polymer and drug were performed for polymer drug interaction studies between 4000 $cm^{-1}$to 400 cm^{-1}.[8]

Preparation of Flunarizine HCl Fast Dissolving Tablets:

Various formulations of fast disintegrating tablets of Flunarizine HCl were prepared by using sublimation method. Accurately weighed quantity of Flunarizine HCl, subliming agents (camphor and menthol), super disintegrating agent (SSG), aspartame, MCC and mannitol were mixed and passed through the sieve no 44. Finally, magnesium stearate and talc were added as lubricating agent. The tablets were prepared by direct compression method using 6mm flat punches on a 10 station rotary compression machine. In all the formulations, the amount of Flunarizine dihydrochloride and superdisintegrants were kept constant and the levels of sublimating agents were varied. After compression tablets were heated in a hot air oven at 60°C for camphor containing batches and at 40^{o}C for batches containing menthol as sublimating agents, until constant weight was obtained to ensure the complete removal of volatilizable component.[9]

The formulation details are given in Table 1.

Table No.1: The Composition Of Fast Dissolving Tablets Of Flunarizine Hydrochloride.

Ingredients	Formulation Code								
	F0 mg	**F1 mg**	**F2 mg**	**F3 mg**	**F4 mg**	**F5 mg**	**F6 mg**	**F7 mg**	**F8 mg**
Flunarizine HCl	5	5	5	5	5	5	5	5	5
SSG	6	6	6	6	6	6	6	6	6
Camphor	-	10	20	30	40	-	-	-	-
Menthol	-	-	-	-	-	10	20	30	40
MCC	37	37	37	37	37	37	37	37	37
Mannitol	85	75	65	55	45	75	65	55	45
Aspartame	2	2	2	2	2	2	2	2	2
Talc	5	5	5	5	5	5	5	5	5
Magnesium sterate	1	1	1	1	1	1	1	1	1
TOTAL	150	150	150	150	150	150	150	150	150

Characterization of Fast Dissolving Tablets:

Evaluation of Blends:

Angle of Repose:

Angle of repose was determined using funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and the angle of repose (ɵ) was calculated using the formula.[10]

$$\theta = \tan^{-1} [h/r]$$

Bulk Density:

Apparent bulk density (pb) was determined by pouring the blend in to a graduated cylinder. The apparent bulk density was calculated using the formula.[11]

$$pb = M/ Vb$$

Where, Vb is the bulk volume and M is the weight of the powder.

Tapped Density:

The measuring cylinder containing a known mass of blend was tapped for 100 tap. The volume occupied in the cylinder (Vt) and the weight (M) of the blend was measured. The tapped density (ρt) was calculated using formula.[11]

$$pt = M/ Vt$$

Compressibility Index:

The simplest way for measuring of free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by compressibility index (I) which is calculated as follows.

$$I = [(pt – pb)/ pt] \times 100$$

Where, pt is the tapped density and pb is tapped volume.

The value below 15% indicates a powder which usually gives rise to good flow characteristics, where as above 25% indicates poor flowability.[11]

Hausner's Ratio:

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following method

$$\text{Hausner ratio} = pt /pd$$

Where pt is tapped density and pd is bulkdensity

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).[11]

Evaluation of Tablets:

Tablet Thickness:

The thickness of three tablets from each batch was determined using a Vernier caliper. The thickness was measured in centimeters.[12]

Tablet Hardness:

The tablet hardness is the force required to break a tablet in a diametric compression force. The hardness tester used in the study was Monsanto hardness tester, which applies force to the tablet diametrically with the help of an inbuilt spring. The hardness was measured in kg/cm^2. Three tablets were taken and their hardness was measured.[13]

Weight Variation:

The procedure described in Indian Pharmacopoeia (IP, 1996)[14] was employed to determine the weight variation of the tablets. Twenty tablets were selected randomly from each batch and weighed individually on electronic balance (Shimadzu). The individual weighed was then compared with average weight for the weight variations.

Friability:

Friability indicates the ability of a tablet to withstand mechanical shocks while handling. Friability of the tablets was determined by using Roche Friabilator and is expressed in percentage (%). Ten tablets were initially weighed (W_i) and placed into the friabilator. The friabilator was operated at 25 rpm for four minutes or run up to 100 revolutions and then the tablets were weighed again (W_f). The loss in tablet weight due to abrasion or fracture was the measure of tablet friability. Percent friability (F) was calculated by using the following formula. % friability of less than 1 % is considered acceptable.[15]

$$F = \{[(W_i) - (W_f)]/ (W_i)\} \times 100$$

Wetting Time:

Five circular tissue papers were placed in a Petri dish of 10 cm diameter. Ten milliliters of phosphate buffer 6.8 containing a water-soluble dye, was added to the petridish. The dye solution was used to identify complete wetting of the tablet surface. A tablet was carefully placed on the surface of the tissue paper in the petridish at 25^0C. The time required for water to reach the upper surface of the tablets and to completely wet them was noted as the wetting time. This test was carried out in replicate of three. Wetting time was recorded using a stopwatch.[16]Wetting time of best formulation is shown in figure. no.1.

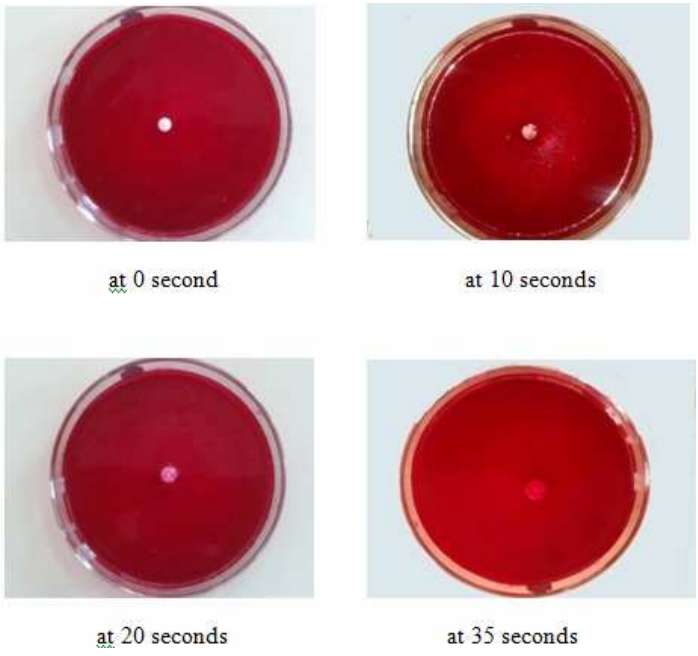

Figure no.1: Wetting time of best formulation (F8) of fast dissolving tablet in dye (amaranth)

Water Absorption Ratio:

A piece of tissue paper folded twice was placed in a Petridish containing 10ml of water. A pre weighed tablet was placed on the paper. The wetted tablet was then weighed. Water absorption ration R was determined according to the following formula.[17]

$$R = (Wa- Wb/ Wb) 100$$

Where, Wa = weight of tablet after absorption of water

Wb= weight of tablet before absorption of water

Drug Content:

Twenty tablets of each batch were weighed and powdered. An amount of powder equivalent to five mg of Flunarizine hydrochloride was dissolved in 100ml of 0.1N HCl, filtered, diluted suitably and analyzed for drug content at 251 nm using UV-Visible spectrophotometer.[18]

***in-vitro* Disintegration Time:**

Disintegration time was measured in 900 ml of 0.1N HCl according to the USP 24 method without disc at 37 ± 0.5^{o}C temperature. The disintegration times of three individual tablets were recorded and the average was reported.[19]

***in-vitro* Dissolution Study:**

The release rates of Flunarizine hydrochloride from fast dissolving tablets were determined using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of 0.1N HCl, at 37±0.5°C and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at regular intervals of 15 seconds for 2.5 mins. The samples were replaced with fresh dissolution medium of same quantity. The samples were filtered through a 0.45µ membrane filter. Absorbance of these solutions was measured at 251 nm using Jasco V- 630 UV Spectrophotometer. Cumulative percentage of drug release was then calculated.[20]

Stability Studies:

In order to determine the change in *In-vitro* release profile on storage, stability studies of optimized batch i.e., F8 was carried out at 40°C in a humidity chamber having 75% RH. Samples were withdrawn at regular intervals of 30 days during the study of 60 days. Formulation is evaluated for change in *In-vitro* drug release pattern, hardness, wetting time, weight variation, percent drug content and dispersion time.[21]

Results

In this work Flunarizine hydrochloride Fast dissolving tablets have been prepared by sublimation method using various sublimating agents such as Menthol and Camphor. SSG has been used as superdisintegrant in its optimum concentration i.e. in 4%w/w in all the formulations. The concentrations of sublimating agents have been varied from 0%-26.5% in different formulations.

Excipients Compatibility Study:

Results of IR spectrum of the pure drug Flunarizine HCl, powder mixture of pure drug and superdisintegrants are represented in figure no.2. The FTIR of best formulation is represented in figure no.3. The flunarizine HCl has indicating presence of C-F bond, C-N bond, aliphatic C=C bond, aromatic C=C bond, C-H bond in the range of 1000cm^{-1} to 1350 cm^{-1},1030 cm^{-1} to 1230 cm^{-1},at 890 cm^{-1}, 730 cm^{-1} to 770 cm^{-1} and 2850 cm^{-1} to 3100 cm^{-1} respectively. These peaks indicating the functional groups in Flunarizine HCl are present in the FTIR spectrum of the drug, physical mixture of the drug and superdisintegrant. Hence, it is concluded that, drug is present in free state in powder mixture, not in the form of reaction product. The specific peak values are shown in table no.2.

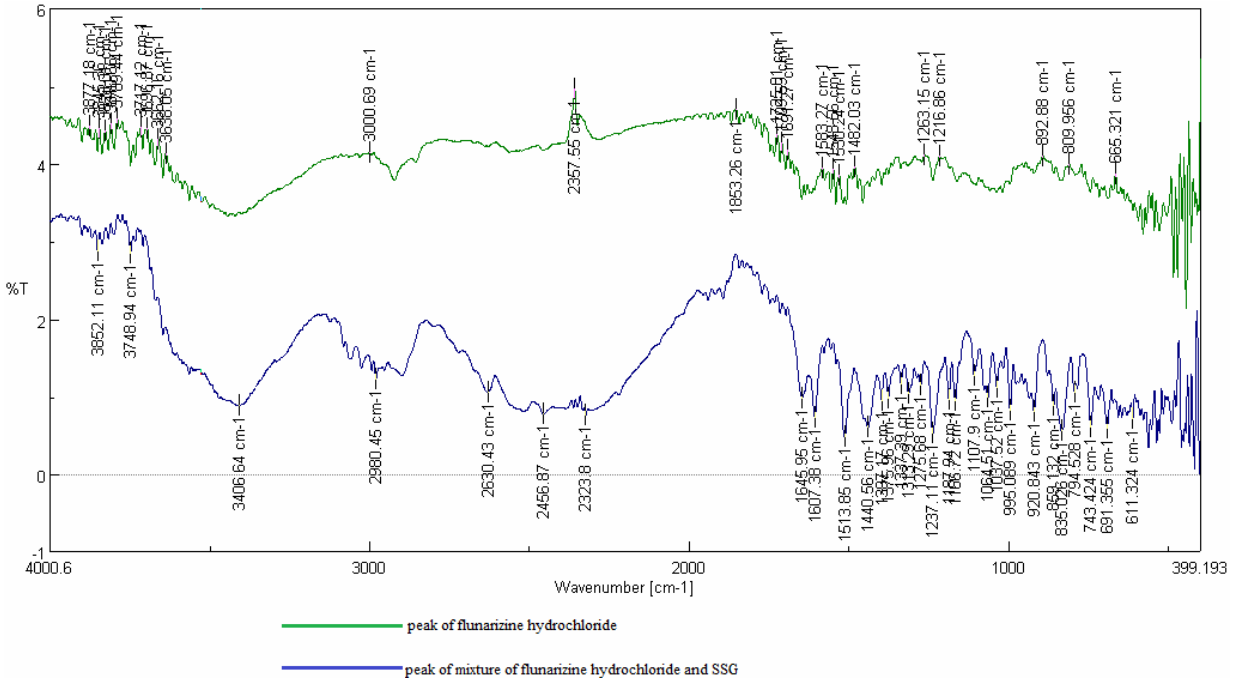

Figure.no.2: FTIR of Flunarizine HCl and Flunarizine HCl + Sodium Starch Glycolate.

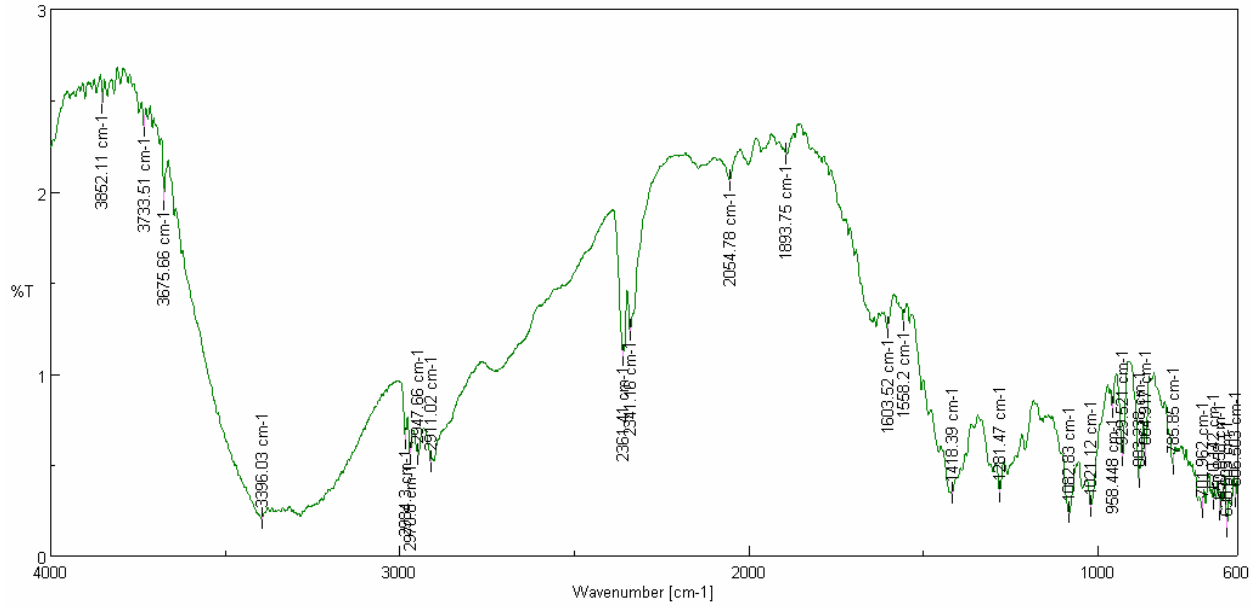

Figure.no.3: FTIR of best formulation (F8).

Table No.2: Ft-Ir Studies Of Flunarizine Hcl Alone And With Excipients

Combinations	Peak of C-F bond (nm)	Peak of C-N bond (nm)	Peak of C=C (aliphatic) bond (nm)	Peak of C=C (aromatic) bond (nm)	Peak of C-H bond (nm)
Flunarizine HCl	1338.36	1038.48	837.91	743.42	2920.66
Flunarizine HCl + SSG	1397.17	1037.52	835.99	743.42	2899.45

Evaluation of Formulated Batches:

The nine formulations prepared by direct compression method were then evaluated for pre compression parameters of the powder blend such as angle of repose, bulk density, tapped density, carr's index and hausners ratio and post compression parameters of the compressed tablets such as hardness, friability, disintegration time, weight variation, thickness, drug content, wetting time, water absorption ratio and *In-vitro* drug release.

The results of pre compression parameters and post compression parameters are tabulated in table no.3 and table no.4 respectively.

Table No.3: Pre Compression Parameters of Powder Blend

Pre Compression Parameters	Formulation Code								
	F0	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
Angle of Repose(θ)*	20.3	21.8	22.2	22.6	23.4	19.6	20.3	20.6	21.4
Bulk Density (gms/cm^3)	0.90	0.88	0.86	0.89	0.88	0.89	0.87	0.90	0.89
Tapped Density (gms/cm3)	0.99	0.98	0.96	1.00	0.99	0.99	0.97	1.01	1.00
Carr's Index (%)	9.0	9.8	10.6	10.9	11.7	9.7	10.5	10.7	11.5
Hausners Ratio	1.10	1.11	1.12	1.12	1.01	1.11	1.12	1.12	1.13

*Values are mean of 3 observations

Table No.4: Post Compression Parameters Of Fast Dissolving Tablets

Post Compression Parameters	Formulation Code								
	F0	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
Thickness ± SD (cm)*	0.34 ±0.01	0.35 ±0.02	0.35 ±0.01	0.34 ±0.01	0.34 ±0.02	0.35 ±0.01	0.35 ±0.01	0.34 ±0.02	0.34 ±0.01
Hardness ± SD (Kg/cm2)*	3.51 ±0.13	3.44 ±0.11	3.39 ±0.12	3.11 ±0.13	2.96 ±0.15	3.02 ±0.13	2.83 ±0.15	2.61 ±0.14	2.55 ±0.15
Weight Variation Test ± SD (mg)**	150.3 ±1.12	140.6 ±1.01	130.9 ±1.18	120.2 ±1.2	110.3 ±1.12	140.1 ±1.16	130.4 ±1.15	120.1 ±1.19	110.9 ±1.2
Friability (%)	0.066	0.199	0.295	0.368	0.488	0.371	0.499	0.541	0.691
Disintegration time ± SD (secs)*	49.30 ±3.3	35.20 ±2.5	30.60 ±2.9	28.40 ±3.9	25.30 ±2.4	31.70 ±2.3	28.40 ±1.6	26.10 ±2.2	22.60 ±2.7
Wetting Time ± SD (secs)*	78.43 ±1.3	57.36 ±1.9	53.81 ±1.4	50.25 ±1.1	42.65 ±1.5	51.18 ±1.3	45.62 ±1.1	40.83 ±1.8	33.92 ±1.7
Water Absorption Ratio ± SD (%)*	71.86 ±2.26	81.04 ±2.91	86.93 ±3.12	91.15 ±2.91	92.16 ±2.46	83.33 ±3.26	88.03 ±3.24	91.16 ±2.96	92.84 ±2.15
Drug Content ± SD (%)*	99.43 ±0.21	98.91 ±0.11	100.05 ±0.26	100.01 ±0.44	99.54 ±0.23	98.99 ±0.19	98.58 ±0.09	100.72 ±0.26	100.86 ±0.06

*Values are mean of 3 observations.
** Values are mean of 20 observations.

***in-vitro* Dissolution Study:**

The In-vitro studies for all the prepared formulations were done in 900ml of 0.1N HCl for 2.5 mins according to the procedure. The results showed that the formulations containing sublimating agents release drug in a faster rate than the rate of release of drug from the formulation without sublimating agents. Formulation using menthol as superdisintegrant in the concentration 26.5%w/w showed better result and complete drug release in 5 mins. The results of the study are tabulated in table no.5.

The %CDR v/s time graph of F0 to F4 formulations and F5 to F8 are plotted in figure no. 4 and figure no.5 respectively. Figure no.4 shows F4 as best formulation and figure no.5 shows F7 as best formulation. To compare these two, another figure, figure no.6 was plotted comparing the release pattern of formulation F4 and formulation F8. From the figure no.6 it was found that the formulation F8 was the best among all the formulations prepared.

Stability Studies:

The stability studies were carried out for 60 days according to procedure. The results of the stability studies are tabulated in table no.6.

Table No.5: Percentage Cumulative Drug Release Of Fast Dissolving Tablets

% Cumulative Drug Release									
TIME(sec)	**F0 (%)**	**F1 (%)**	**F2 (%)**	**F3 (%)**	**F4 (%)**	**F5 (%)**	**F6 (%)**	**F7 (%)**	**F8 (%)**
0	0	0	0	0	0	0	0	0	0
30	18.28	34.32	36.25	39.52	41.09	36.59	38.58	41.85	43.95
60	23.36	39.06	42.53	45.08	48.94	43.03	46.49	49.74	52.03
90	30.09	44.49	46.99	49.39	54.63	46.39	50.29	54.04	56.88
120	37.02	52.65	54.86	58.91	62.81	53.84	57.93	60.74	65.62
150	45.27	59.99	62.87	66.03	69.89	61.64	65.27	68.03	72.28
180	51.98	63.01	65.82	69.93	73.31	66.02	68.27	71.93	76.33
210	60.43	69.81	71.89	75.91	79.43	72.64	74.38	77.94	81.85
240	67.09	75.81	78.63	82.83	85.18	78.28	81.86	85.38	88.91
270	70.91	79.99	83.89	86.91	89.43	82.28	86.93	89.63	92.26
300	74.96	82.74	88.63	90.83	96.18	86.28	91.57	93.94	99.92

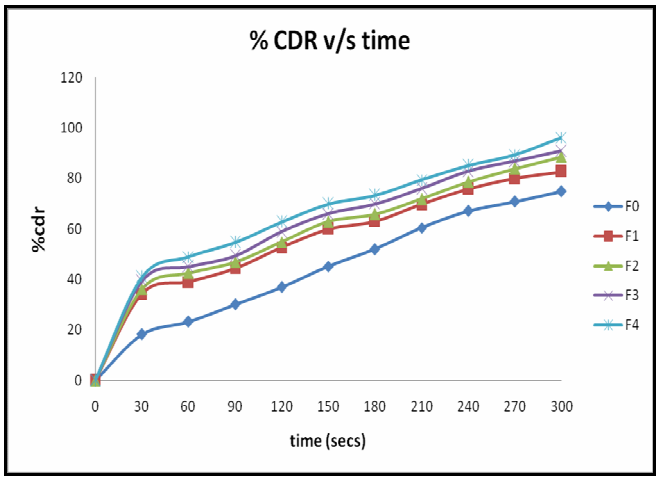

Figure.no.4: dissolution profile of fast dissolving tablets F0 – F4.

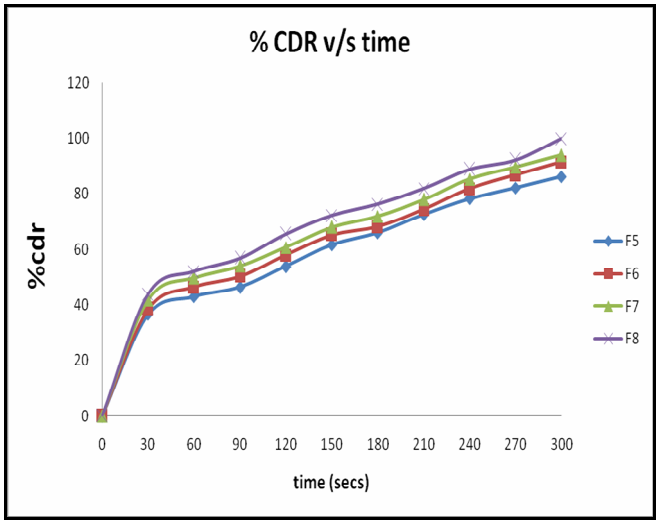

Figure.no.5: dissolution profile of fast dissolving tablets F5 – F8.

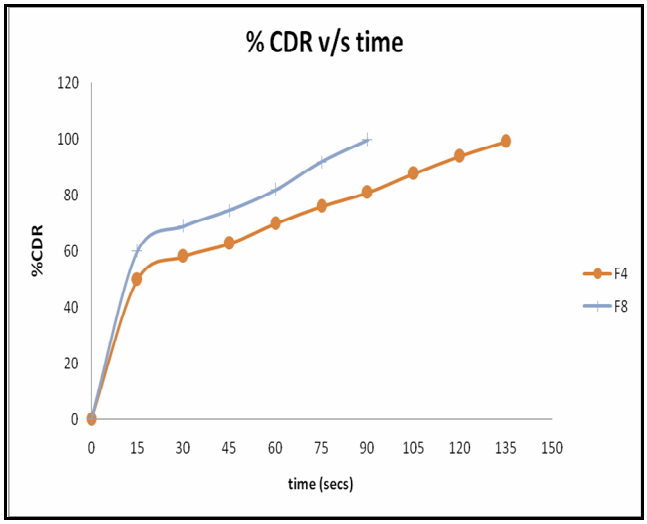

Figure.no.6: dissolution profile of fast dissolving tablets F4 and F8.

Table No.6: Stability Studies Of Best Formulation F8.

Parameters	**At 0 days**	**At 30 days**	**At 60 days**
Hardness ± SD (Kg/cm2)*	2.55±0.15	2.01±0.19	2.00±0.14
Wetting time ± SD (secs)*	33.92±1.7	34.72±1.1	36.09±1.3
Weight variation ± SD (mg)**	110.9±1.2	112.9±1.0	114.9±1.9
Disintegration time ± SD (secs)*	22.60±2.7	24.02±2.1	25.51±2.9
Percent drug content ± SD (%)*	100.86±0.06	99.06±0.26	98.96±0.03
In-vitro drug release at 5 mins± SD (%)*	99.92%	99.07%	98.86%

*Values are mean of 3 observations.
** Values are mean of 20 observations.

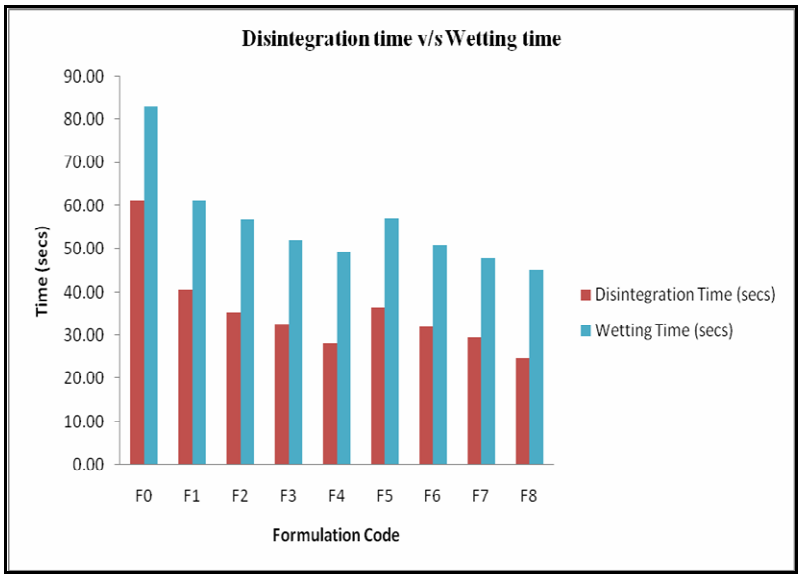

Figure no.7: comparison of disintegration time and wetting time of formulations.

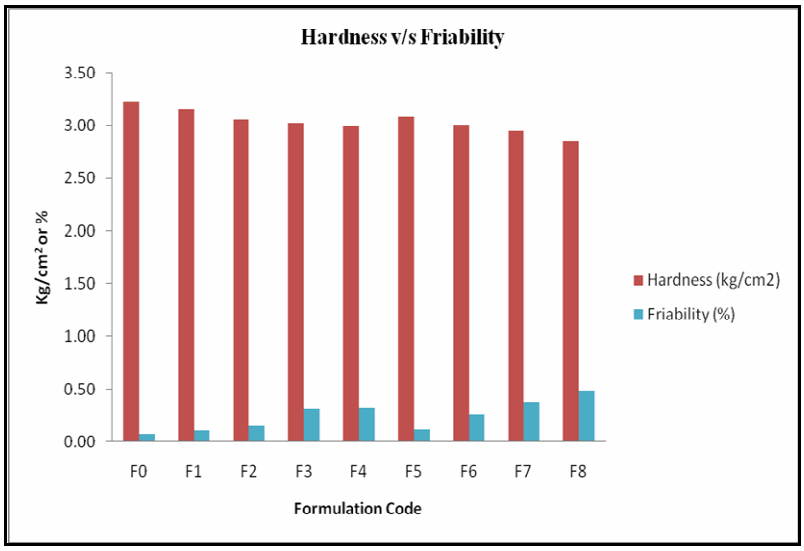

Figure no.8: comparison of hardness and friability of formulations.

Discussions

The results of formulation F0, with no sublimating agents, showed poor post compression parameters, so sublimation technique was used to formulate fast dissolving tablets using camphor and menthol as sublimating agents, thus to produce porous structure in the tablet matrix.

The pre compression parameters of all the formulations didn't show any significant variations which may be influenced by the addition of sublimating agents. It is worthwhile to note, that the addition of camphor and menthol also resulted in increased friability and low hardness probably due to the generation of the porous structure in the tablet matrix. But they were found to be in their limits as in IP 1996. The wetting time and dispersion time of the formulations where decreased as the concentration of the sublimating agents increased. The cumulative drug releases were also increased in each time interval according to the increase in the concentration of sublimating agents. The stability studies showed that the best formulation F8 didn't show any significant variations in their specific post compression parameters. So it was concluded that the best formulation was stable for a time period of 60 days.

Yet another discussion was that, as the sublimating agent used in this study, menthol, was found to be the best compared to camphor, it has another advantage of pleasant mouth feel. It is an additional advantage in case of the fast dissolving tablets prepared in the study.

From the above work it was concluded that formulation F8 showed maximum drug release within 5 mins when compared to all other formulation. As all the other parameters of the formulation F8 were also excellent, the concentration of menthol which is used in F8 formulation was found ideal for the sublimation method. Hence the present formulation of fast dissolving tablet of Flunarizine HCl by sublimation method using menthol as sublimating agent and SSG as superdisintegrant can be used for better patient compliance.

References

1. Bankim CN, Bhaskar M, Kadambari P, Nidhi S, Swati J, Stuti S *et al.* An overview on fast dissolving drug delivery system. Asian Journal of Pharmaceutical Sciences and Research 2011 Jul; 1(2):1-30.
2. Albert RR, Josep PF, Jordi GC, Joan HN, Maite AF, Elia GH. Acceptance survey of a fast dissolving tablet pharmaceutical formulation in allergic patients. Satisfaction and expectancies. Allergol Immunopathol 2006; 34(3):107-12.
3. Himanshu D, Chandrashekhara S, Nagesh C, Amol M, Shridhar U. Superdisintegrants: A Recent Investigation and Current Approach. Asian J Pharm Tech 2012; 2(1):19-25.
4. Mohit M, Sunil T, Manish G, Pankaj G. Superdisintegrants: An Updated Review. International Journal of Pharmacy and Pharmaceutical Sciences Research 2012; 2(2):26-35.
5. Alok KG, Anuj M, Jha KK. Fast Dissolving Tablet- A Review. The Pharma innovation 2012; 1(1):1-8.

6. Doddayya H, Shrishail SP, Pallavi B. Comparative evaluation of selected superdisintegrants on the release of Flunarizine Dihydrochloride from mouth dissolving tablets. RGUHS J Pharm Sci 2012 Oct-Dec; 2(4):50-7.
7. Mohit M, Sunil T, Manish G, Pankaj G. Superdisintegrants: An Updated Review. International Journal of Pharmacy and Pharmaceutical Science Research 2012; 2(2) 26-35.
8. Sudarshan S, Dhaval S. Development and Characterization of Mouth Dissolving Tablet of Zolmitriptan. Asian Pacific Journal of Tropical Disease 2012; 457-64.
9. Kalpesh G, Lalit KT, Kori ML, Sharma CS, Nema RK. Formulation and Characterization of Fast Disintegrating Tablet of Aceclofenac by using Sublimation Method. International Journal of Pharma ceutical Sciences and Drug Research 2011; 3(1):19-22.
10. Prameela RA, Aarchana N, Siva TP, Mohan VP, Sudheer KM, Bala SC. Formulation and Evaluation of Orodispersible Metformin Tablets: a Comparative study on isphagula husk and crosspovidone as superdisintegrants. International Journal of Applied Pharmaceutics 2010; 2(3):15-21.
11. Adimoolam S, Chidambaram S, Inampudi A, Vontoor BN, Juvva MK. Formulation and evaluation of mouth dissolving tablets of flunarizine dihydrochloride by using super disintegrants. International Research Journal of Pharmacy 2010; 1(1):267-76.
12. Chetan GP, Shivprasad HM. Comparative Success of Natural Superdisintegrant over Synthetic Superdisintegrants in Fast Disintegrating Tablets. Asian Journal of Biomedical and Pharmaceutical Sciences 2012; 2(12):69-72.
13. Ankur S, Abhishek J, Anuj P, Rakesh J, Sheorey RV. Formulation and evaluation of aceclofenac fast dissolving tablets. International Journal of Pharmacy and Life Sciences 2011 Apr; 2(4):681-6.
14. Indian Pharmacopoeia. Ministry of Health and Family Welfare. Government of India, Vol II, Delhi, 1996, p.350.
15. Kalpesh G, Lalit KT, Kori ML, Sharma CS, NemaRK. Formulation and Characterization of Fast Disintegrating Tablet of Aceclofenac by using Sublimation Method. International Journal of Pharmaceutical Sciences and Drug Research 2011; 3(1):19-22.
16. Chandrasekhar P, Sreenivas PS, Bibhu PP, Bhanoji RME. Formulation and Evaluation of Cetirizine HCl Mouth Fast Dissolving Tablets. Der Pharmacia Lettre 2011; 3(4):63-70.
17. Harish C, Sachin K, Bineeta B. Formulation and evaluation of fast dissolving tablet of Ramipril. Der Pharmacia Sinica 2011; 2(6):153-60.
18. Kavitha K, Sandeep DS, Mehaboob Y, More M. Formulation and Evaluation of Oral Fast Dissolving Tablets of Promethazine HCl by Sublimation Method. International Journal of Pharm Tech Research 2011; 3(2):660-3.
19. Jain CP, Naruka PS. Formulation and Evaluation of Fast Dissolving Tablets Of Valsartan. International Journal of Pharmacy and Pharmaceutical Science 2009 Jul-Sep; 1(1):219-26.
20. Sudheshnababu S, Sai KV. Formulation and evaluation of fast dissolving tablets of amlodipine besylate by using Fenugreek seed mucilage and Ocimum basilicum gum. International Current Pharmaceutical Journal 2012; 1(9): 243-9.
21. Rohan DD, Gowda DV, Vasanti S, Mahammed N, Maramwar DN. Design and evaluation of mouth dissolving tablets of ebastine by sublimation technique. Der Pharmacia Lettre 2011; 3(4):193-9.

*****