Available online at www.scholarsresearchlibrary.com

Scholars Research Library

Der Pharmacia Lettre, 2017, 9 [9]:34-44
[http://scholarsresearchlibrary.com/archive.html]

Scholars Research Library
ISSN 0975-5071
USA CODEN: DPLEB4

Formulation and Evaluation of Hydralazine Hydrochloride Fast Dissolving Tablets by Sublimation Method In the Treatment of Pregnancy Induced Hypertension

MUTHUKUMAR S[1*], SUNDARA GANAPATHY R[2]

[1]*Research Scholar, Karpagam Academy of Higher Education, Karpagam University, Coimbatore-21, Tamil Nadu, India.*

[2]*Faculty of Pharmacy, Karpagam Academy of Higher Education, Karpagam University, Coimbatore-21, Tamil Nadu, India.*

***Corresponding author:** Muthukumar S, Research Scholar-Faculty of Pharmacy, Karpagam Academy of Higher Education, Karpagam University, Coimbatore. Email:pharmmuthu@gmail.com*

ABSTRACT

Solid dosage forms also have a impervious difficulties in patients especially for geriatric and paediatric patients.Dysphagia is common among all age groups.Fast dissolving tablets constitute an inventive dosage form that overcome the problems swallowing and provides speedy onset of action.The objective of present study was to formulate FDTs of Hydralazine HCL by sublimation method. Formulation of FDTs of Hydralazine HCL were prepared by using various superdisintegrants and volatile ingredients. The formulas were evaluated for compatibility, Pre-compression studies and post compression studies. Optimised formula was subjected to stability studies.Among all the formulations SF9 showed effective percentage of drug release at 12 minutes.

Keywords: Fast dissolving tablet, Pregnancy induced hypertension (Eclampsia and preeclampsia), Hydralazine Hydrochloride, sublimation method.

INTRODUCTION

Tablet is the familiar dosage form because of patient convenience prefer for paediatric, geriatric population. To overcome this problem scientist has developed NDDS known as fast dissolving tablets [1-2]. The FDTs as a solid dosage form containing medicinal substances, which disintegrates rapidly, usually with in a seconds, when placed upon the tongue provides quick onset of action, enhanced bioavailability [3].

Sublimation Method has been used to produce fast dissolving tablets with high porosity by compressing the volatile materials along with other excipients in to tablets, which are finally subjected to a process of sublimation. The removal of the volatile materials by heating under vacuum there by porosity is reached due to the formation of many pores. These compressed tablets which have porosity fast dissolved within 15seconds in saliva [4-5].

Hypertension, complicating 5% to 7% of all pregnancies, is a leading cause of maternal and fetal morbidity, particularly when the elevated blood pressure (BP) is due to preeclampsia [6]. Pre-eclampsia is a medical condition characterized by high blood pressure and significant amounts of protein in the urine of a pregnant women. If left untreated, it can develop into eclampsia, the life-threatening occurrence of seizers during pregnancy [7-8].

MATERIALS AND METHODS

Active Pharmaceutical Ingredients was procured from Octopus pharmaceuticals, Chennai. Superdisintegrants Other excipients were purchased from Himedia Ltd.

Preparation of Fast dissolving tablets by Sublimation method [9]

FDTs prepared by using Volatile ingredients and super disintegrants such as, crospovidone, CCS, SSG in varying ratios. Tablets were prepared by using camphor(Volatile Ingredient) in different ratios. All the ingredients were passed through #60 separately. Then the ingredients were weighted and mixed in geometrical order and the tablets were compressed using 8mm size punch.The compressed tablets were then subjected to sublimation at 60˚C for 1 hour. Compositions of different formulations were given in **(Table 1,2)**.

Table 1: Formula fast dissolving tablets of hydralazine hydrochloride by sublimation method [18]

S.No	Ingredients Used	Formulation code								
		SF1	SF2	SF3	SF4	SF5	SF6	SF7	SF8	SF9
01.	Hydralazine HCL	50	50	50	50	50	50	50	50	50
02.	Crospovidone	6	8	10	-	-	-	-	-	-
03.	CCS	-	-	-	6	8	10	-	-	-
04.	SSG	-	-	-	-	-	-	6	8	10
05.	Aspartame	5	5	5	5	5	5	5	5	5

06.	Mannitol	50	50	50	50	50	50	50	50	50
07.	Mg.Stearate	2	2	2	2	2	2	2	2	2
08.	Camphor	2	4	6	2	4	6	2	4	6
09.	MCC	83	80	77	83	80	77	83	80	77
10.	Talc	2	2	2	2	2	2	2	2	2
Weight of the tablet		**200 mg**								

Compatibility Studies [10-11]

Differential Scanning Colorimetry (DSC) & Thermogravimetric analysis (TGA)

DSC and TGA were performed for API and selected formulations.

Evaluation

Pre-Compression Parameters [11]

The tablet blends were evaluated for their bulk density, tapped density, Carr's index and flow properties.

Postcompression parameters [12-16]

The compressed tablets were evaluated for the tests such as weight variation, thickness, hardness, friability, D.T an dissolution studies as per the pharmacopoeia standards and also specific tests like wetting time and water absorption ratio were performed.

Stability Studies [17]

Stability studies of the selected formula kept for stability as per the ICH guidelines under accelerated condition 40± 0.2º C/75± 5% RH.

RESULTS AND DISCUSSION

DSC and TGA graph shown in **Figure-1, Figure-2** of the drug and the tablet blend shows no extra peaks. Hence it can be concluded that there was no physical interaction of drug and the excipient.

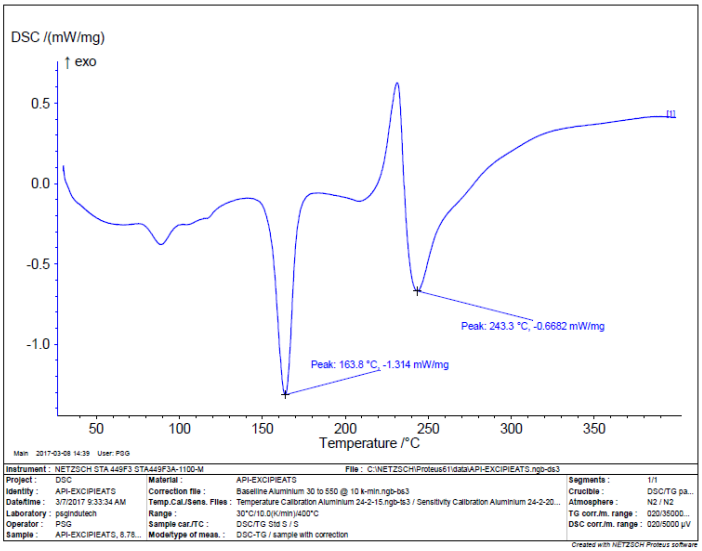

Figure 1: DSC of FDTs prepared by sublimation method

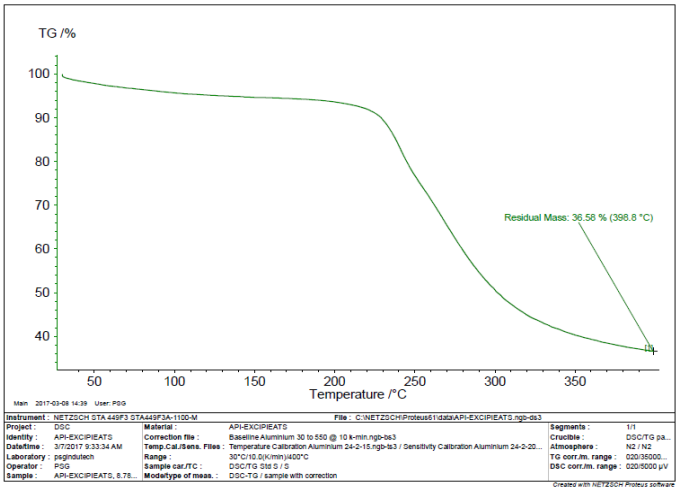

Figure 2: TGA of fast dissolving tablets by sublimation method.

Pre-Compression parameters [18]

Table 2: Pre-Compression parameters

Batch code	Angle of repose (θ)	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Carr's Index (%)	Hausner's Ratio
API	26.27±0.13	0.31±0.03	0.36±0.01	13.88±0.33	1.16±0.04
SF1	31.21±0.16	0.29±0.01	0.34±0.01	14.70±0.23	1.17±0.02
SF2	28.48±0.24	0.31±0.10	0.37±0.04	16.21±0.27	1.19±0.09
SF3	33.16±0.17	0.29±0.02	0.33±0.02	12.12±0.06	1.13±0.03
SF4	30.79±0.14	0.33±0.03	0.39±0.01	15.38±0.85	1.18±0.05
SF5	30.27±0.19	0.31±0.11	0.36±0.03	13.88±0.67	1.16±0.02
SF6	29.13±0.14	0.34±0.01	0.40±0.03	15.00±0.31	1.17±0.04
SF7	31.08±0.13	0.33±0.04	0.37±0.02	10.81±0.13	1.12±0.06
SF8	32.26±0.21	0.31±0.03	0.35±0.01	11.42±0.26	1.12±0.01
SF9	33.41±0.22	0.34±0.02	0.38±0.04	10.52±0.09	1.11±0.03

The data obtained for pre-compression parameters are shown in **Table-2** were found to be within the prescribed limits and indicated good free flowing properties.

Table 3: Post Compression parameters [18]

	FORMULATION CODE								
Parameters	**SF1**	**SF2**	**SF3**	**SF4**	**SF5**	**SF6**	**SF7**	**SF8**	**SF9**
Weight variation test (mg)	199± 0.34	200± 1.34	199± 0.67	198± 0.47	201± 0.34	200± 0.34	198± 1.45	200± 0.57	201± 0.34
Thickness (mm)	2.81±0.12	2.72± 0.34	3.28± 0.41	2.94± 0.23	3.25± 0.34	2.90± 0.98	3.16± 0.99	2.68± 0.34	3.02± 0.45
Hardness test (kg/cm^3)	2.68± 0.35	3.41± 0.87	2.78± 1.34	3.45± 1.58	2.90± 0.46	2.78± 0.47	3.07± 0.33	2.99± 1.23	3.34± 0.47

Friability (%)	0.56± 0.11	0.63± 0.24	0.51± 0.45	0.87± 0.34	0.70± 1.57	0.56± 0.34	0.75± 0.11	0.66± 2.34	0.74± 0.87
Disintegration time (sec)	25± 0.34	31± 0.34	27± 1.34	30± 0.89	28± 0.33	30± 0.47	29± 0.48	32± 0.34	34± 0.93
Wetting time (sec)	37± 0.23	41± 0.36	28± 0.45	38± 0.35	34± 0.33	37± 0.78	41± 0.78	35± 0.35	40± 0.37
Water absorption (%)	70± 0.67	69± 1.34	82± 1.40	79± 1.20	76± 0.61	85± 0.99	81± 0.56	74± 0.36	70± 0.46
Drug content (%)	89± 0.55	96± 0.89	87± 0.16	94± 0.56	96± 0.45	89± 0.41	96± 0.48	91± 0.11	87± 0.38

All the post compression parameters are mentioned in **Table-3, Table-4 and Figure-3** were within the IP acceptable limits. The tablets weight variation for the optimised formulation SF9 of Fast dissolving tablets prepared by Sublimation method was measured in the range of 201±0.34 mg . Thickness was in the range of 3.02±0.45 hardness in the range of 3.34±0.47 kg/cm2. The percentage friability was less than 1% for all formulations ensuring mechanical stability of the formulated tablets.

All formulations were evaluated for percentage drug content and found in the range of 87 ± 0.38 indicating the compliance with the Pharmacopoeia limits. According to the Pharmacopoeia standards the dispersible tablet must disintegrate within 3 min, but all formulated batches have shown very low disintegration time i.e. 34± 0.93seconds indicating suitability of formulation for fast dissolving tablet. Wetting time found in the range of 40±0.37 Seconds, water absorption ratio was 70±0.46 percentages. In vitro study was found to be optimum for the formulation SF9 in the range of 99.98±0.77 percentage at 12 mins.

Table 4: Comparative *In-vitro* Dissolution study of FDTs [18]

	TIME(min)						
Formulation code	**0**	**2**	**4**	**6**	**8**	**10**	**12**
SF1	5.34±0.3	23.34±14	38.64±0.34	51.43±0.12	72.95±0.246	87.13±0.84	98.31±0.58
SF2	6.16±0.12	20.67±12	41.40±0.24	46.80±0.05	68.80±0.435	86.89±0.77	96.00±0.42
SF3	6.16±0.71	20.67±45	41.40±0.67	46.80±0.71	68.80±0.81	86.89±0.43	96.00±0.54
SF4	9.46±1.5	24.16±0.58	40.22±0.23	59.34±0.23	76.50±0.36	83.90±0.38	96.08±0.43
SF5	7.25±21	23.89±0.76	39.73±0.58	47.89±0.24	64.80±0.58	78.33±0.86	95.29±0.62
SF6	8.34±0.9	23.34±0.45	33.16±16	51.43±0.47	66.19±0.34	79.24±0.51	79.24±0.34
SF7	7.83±0.58	23.610.47	37.82±0.74	46.80±0.61	72.70±0.71	85.11±0.72	98.04±0.71

SF8	8.01±0.12	19.74±0.87	45.46±0.57	60.18±0.12	79.52±0.34	87.45±0.28	100.74±0.52
SF9	7.83±0.23	22.39±0.98	41.34±0.34	52.55±0.58	71.37±14	87.76±0.66	99.98±0.77

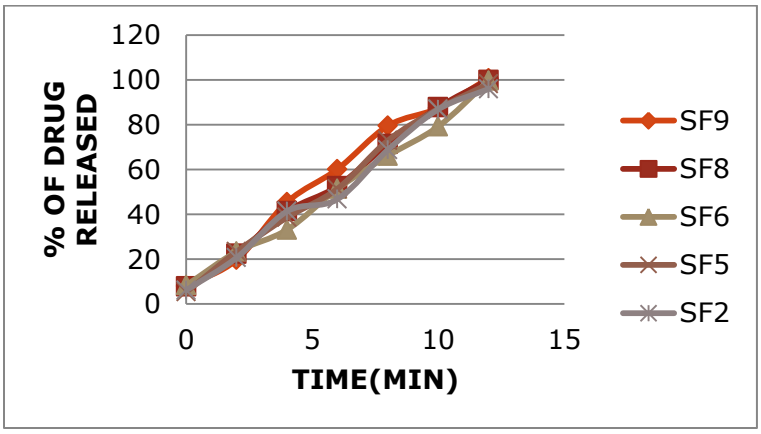

Figure 3: Comparative *In-vitro* Dissolution study

Table 5: Stability study

S.No	Parameters	Initial	Stored at 40˚C±2˚C and 75%±5% RH					
			In month					
			1	2	3	4	5	6
1	Description	White colour	White colour	White colour	White colour	White colour	White colour	White colour
2	Average weight (mg)	200	200	199.90	199.28	200	199.90	199.28
3	Friability (%)	0.20	0.20	0.20	0.20	0.20	0.20	0.20
4	Hardness (kg/cm^2)	3.9	3.0	2.9	2.9	3.0	2.9	2.9
5	Disintegration time (sec)	13	13	14	15	13	14	15

6	Drug content (%)	99.99	99.90	99.82	99.80	99.90	99.82	99.80

Table 6: Comparative *In-vitro* dissolution profile before and after storage at 40˚C±2˚C and 75%±5% RH

Time in minutes	**Cumulative % of drug release (±S.D) n=6**						
	Initial	**1st month**	**2nd month**	**3rd month**	**4th month**	**5th month**	**6th month**
0	0	0	0	0	0	0	0
2	22.13 ± 0.25	22.01 ± 0.26	22.00 ± 0.14	21.88 ± 0.54	21.81 ± 0.58	22.48 ± 0.53	21.65± 0.49
4	57.38 ± 0.47	57.28 ± 0.40	57.04 ± 0.26	56.92 ± 0.24	57.67 ± 0.05	57.62 ± 0.67	56.75± 0.83
6	77.52 ± 0.15	77.50 ± 0.14	76.98 ± 0.11	76.62 ± 0.82	76.55 ± 0.62	76.85 ± 0.95	76.22 ± 0.63
8	89.20 ± 0.32	89.12 ± 0.24	88.92 ± 0.14	88.82 ± 0.45	89.37 ± 0.56	88.24 ± 0.48	88.32 ± 0.66
10	93.78 ± 0.98	93.44 ± 0.72	93.01 ± 0.26	92.42 ± 0.58	92.42 ± 0.52	92.01 ± 0.71	92.12 ± 0.55
12	98.20 ± 0.1	98.10 ± 0.14	97.92 ± 0.12	97.89 ± 0.18	97.63 ± 0.81	97.73 ± 0.84	97.28 ± 0.92

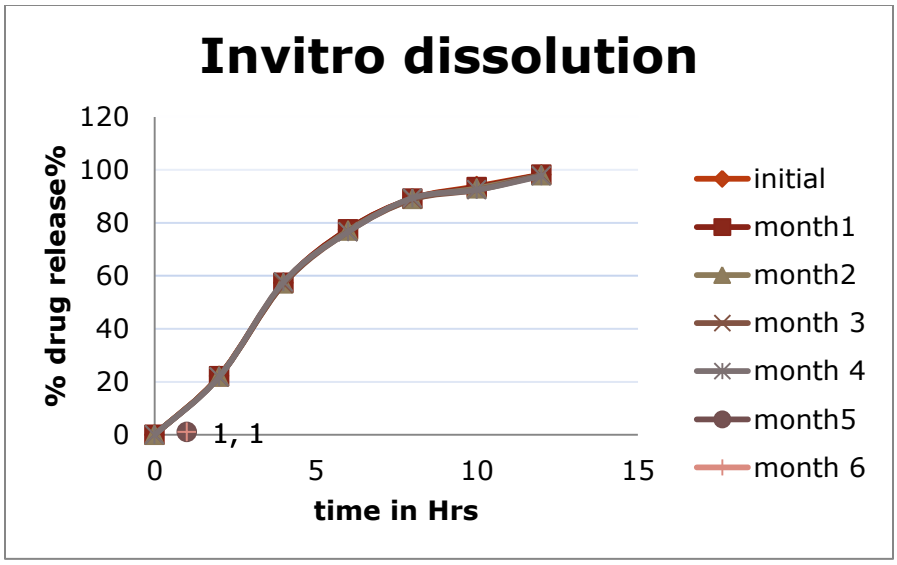

Figure 4: Comparative *In-vitro* dissolution profile storage at 40˚C±2˚C and 75%±5% RH.

Stability results represented in **Table-5, Table-6** and **Fig-4** also indicated that the optimised formulation SF9 shows good stability under accelerated condition.

CONCLUSION

SF9 concluded as optimized and stable formulations from the results of post compression parameters with an effective percentage of drug release at 12 minutes indicating faster and maximum absorption at the site of administration.

ACKNOWLEDGEMENT

The authors are thankful to the managing trustee Karpagam institutions. We are thankfull to Faculty of Pharmacy ,Karpagam Academy of Higher education, Karpagam University, Pollachi road, Coimbatore for providing us the facilities for carrying out the research work.

REFERENCES

1. Tejvir, K., et al. International *Journal of Current Pharmaceutical Research*, **2011.** 3:1-7.
2. Gupta, AK., and Mittal, A., *The Pharm Innovation.* **2012.** 1:1-8.
3. Shasi, SR., et al. *Asian Journal of Pharmaceutics*. **2009.** 3:104-112.

4. Prajapathi, B., and Ratnakar, N., *International Journal of Pharmatech Research.* **2009.**1:790-798.
5. Hirani, JSJ., Rathod, DA., and Vadalia, KR., *Topical Journal of Pharmaceutical Research*. **2009.** 8:161-172.
6. Marshall, D., Lindheimer, MD., Sandra, J., Hypertension in pregnancy. *Journal of American Society of Hypertension,* **2008.** 2(6): 484-494.
7. www.wikipedia.org/wiki/Preeclampsia
8. www.wikipedia.org/wiki/Eclampsia
9. Shukla, D., et al. Mouth Dissolving Tablets I: An Overview of Formulation Technology. *Sci Pharm,* **2009.** 77: 309- 326.
10. Bourne, DW., Pharmacokinetics. In: Banker GS, Rhodes CT, Modern Pharmaceutics, 4th edition. New York, Ny: Marcel Dekker Inc, **2002.** 67-92.
11. General Notice Page No.07 Indian Pharmacopeia 1996 Volume-01 Published by the controller of publication civil line delhi.
12. Devendra, RR., et al.Formulation and evaluation of fast dissolving tablets of Albendazole. *Int Curr Pharm J,* **2012.** 1(10): 311-316.
13. Patel, CJ., et al. Formulation and evaluation of orodispersible tablets of Diazepam using different superdisintegrants. *Int Res J Pharm,* **2012.** 3(3): 298-301.
14. Raghavendra, NG., et al. Development and evaluation of fast dissolving tablets of Fosinopril by sublimation method. *Int J Pharm Sci Drug Res,* **2012.** 4(4): 230-235.
15. Bhunia, B., Varun, j., Formulation and evaluation of orodispersible tablet of Amlodipine besylate. *Int J Pharm Tech,* **2011.** 3(4): 3745-3766.

16. Amitesh, KP., et al. Formulation and evaluation of mouth dissolving tablets of Chlorpromazine HCL. *Int J Pharm Biological Archives.*
17. David J. Mazzo. "International stability testing". Inter pharm press, Banglore; 1-13.
18. Muthukumar, S., and Sundara, GR., Design and Evaluation of Hydralazine Hydrochloride Mouth Dissolving Tablet For the Management of Hypertension. International Journal of Recent Scientific Research. **2017.** 8(5):17230-17235.