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FORMULATION AND EVALUATION OF HYDRALAZINE HYDROCHLORIDE MOUTH DISSOLVING TABLET FOR THE MANAGEMENT OF ECLAMPSIA AND PRE-ECLAMPSIA

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Keywords:

Mouth Dissolving Tablet, Eclampsia, Pre-Eclampsia, Hydralazine Hydrochloride

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ABSTRACT: Eclampsia and Pre-Eclampsia is an acute and life-threatening complication during pregnancy. Hydralazine hydrochloride is one of the drugs of choice in treating this condition. The purpose of the present research work was to formulate the Mouth Dissolving Tablets by using different methods and provide a suitable patient convenience dosage form to enhance the bioavailability and provide quick onset of action. Formulation of MDTs of Hydralazine hydrochloride were prepared by using various superdisintegrants like cross-povidone, cross-carmellose sodium and sodium starch glycolate by direct compression method and camphor as an excipient by sublimation technique. Among all the formulations F9 and SF9 showed effective percentage of drug release at 12 minutes indicating faster and maximum absorption at the site of administration.

INTRODUCTION: A novel dosage form for oral administration. When placed in mouth, disintegrates rapidly or dissolves in saliva, within a few seconds. MDTs usually dissolve in oral cavity within 15 seconds to 3 minutes. Formulation is especially designed for Dysphasic, geriatric, paediatric, bed-ridden, during travelling, Psychotic patients, Unable to swallow or refuse to swallow conventional oral formulations [1, 2]. Among the oral delivery, tablets is the most popular because of convenience of self administration, compactness and easy manufacturing [3]. Sublimation Method has been used to produce MDTs with high porosity by compressing the volatile materials along with other excipients in to tablets,

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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 15 seconds in saliva [4]. 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].

Preeclampsia is a major cause of preterm birth and an early marker for future cardiovascular and metabolic diseases. 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]. Hydralazine Hydrochloride drugs are suitable and effective for the treatment of hypertension because it's having a phthalazinone hydrazone hydrochloride chemical

group. It has a bioavailability of 30% to 60%, T_{max} 1 to 2 hours. Maximum dosing of Hydralazine Hydrochloride is 300 mg / day. It enhances the bioavailability resulting from bypassing the first pass effect [9].

MATERIALS AND METHODS: The drug Hydralazine Hydrochloride was obtained from Octopus pharmaceuticals, Chennai. Croscarmalose sodium, Crospovidone, Sodium starch glycolate, Aspartame, Mannitol, Magnesium stearate, Micro crystalline cellulose, Talc, Camphor were procured from Himedia Ltd., Goa and all other excipient used were analytical grade.

Preformulation Studies: Preformulation studies such as physical appearance, solubility, melting point, hygroscopicity and drug excipient compatibility were performed to confirm the suitability and stability of drug and excipient for the formulation of mouth dissolving tablets [10].

Compatibility Studies: IR studies: IR spectra for pure drug and powdered tablets were recorded in Infrared spectrophotometer with KBr pellets [11].

DSC and TGA: Differential scanning calorimeter and Thermo Gravimetric Analysis were performed for drug and the formulated tablets.

Pre-compression Studies: Pre - Compression parameters like Angle of Repose, Bulk density, tapped density, Compressibility index and Hauser ratio were performed as per the standard procedures [12].

Formulation and Development:

Method A:

Formulation of Mouth Dissolving Tablet by Direct Compression Method: Tablets were prepared by direct compression method using super disintegrants such as, crospovidone, croscarmellose sodium and sodium starch glycolate in varying ratios. All the materials were passed through #60 mesh prior to mixing for uniformity in particle size. The drug and microcrystalline cellulose were mixed using glass mortar and pestle in a small portion of both at each time and blended to get a uniform mixture and kept aside. Then the other ingredients were weighed and mixed in a geometrical order and the tablets were compressed using 8mm size punch to get 200 mg weight using ten stations Rimek tablet punching machine. Compositions of different formulations were prepared by direct compression method [13].

Method B:

Preparation of Mouth Dissolving Tablet by Sublimation method: Tablets were prepared by using camphor in different ratios. All the ingredients were passed through #60 mesh separately. Then the ingredients were weighted and mixed in geometrical order and the tablets were compressed using 8mm size punch to get 200 mg weight using ten stations Rimek tablet punching machine.

The compressed tablets were than subjected to sublimation at 60 °C for 1 hour. Compositions of different formulations were prepared by sublimation technique [14].

Evaluation of Hydralazine Hydrochloride Mouth Dissolving Tablets: The compressed tablets were evaluated for the tests such as weight variation, thickness hardness, friability, *in vitro* disintegration and *in vitro* dissolution rate as per the pharmacopoeia standards and specific tests for the evaluation of mouth dissolving tablets like wetting time and water absorption ratio were performed [15 - 18].

Stability Studies: Stability studies of the formulated orodispersible tablets were performed as per the ICH guidelines under accelerated condition 40 ± 0.2 °C / 75 ± 5% RH and evaluated for its stability [19].

RESULTS: Hydralazine hydrochloride appeared white, odourless, amorphous, and soluble in water with a melting point of 172 ± 0.1 °C.

The FTIR spectra, DSC and TGA of the drug, polymer and physical mixtures of various formulations were compared with the spectra of pure drug and individual excipient in which there was no significant change in the spectrum was observed in **Fig. 1, Fig. 2, Fig. 3, Fig. 4, Fig. 5, Fig. 6** and **Fig. 7** indicating the compatibility of the drug and excipients. Also, no extra peaks were observed other than normal peaks in the spectra of the mouth dissolving tablets which confirms the stability of the formulations.

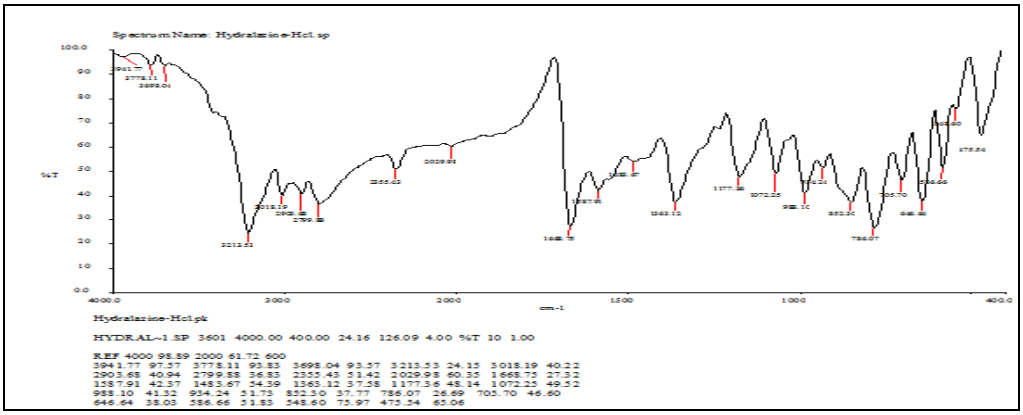

FIG. 1: FTIR SPECTRUM OF HYDRALAZINE HYDROCHLORIDE

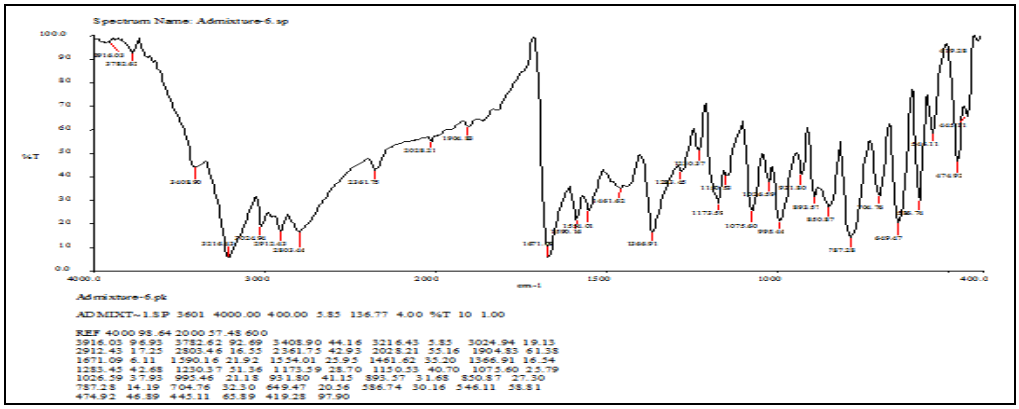

FIG. 2: FTIR SPECTRUM OF MDTs PREPARED BY DIRECT COMPRESSION METHOD

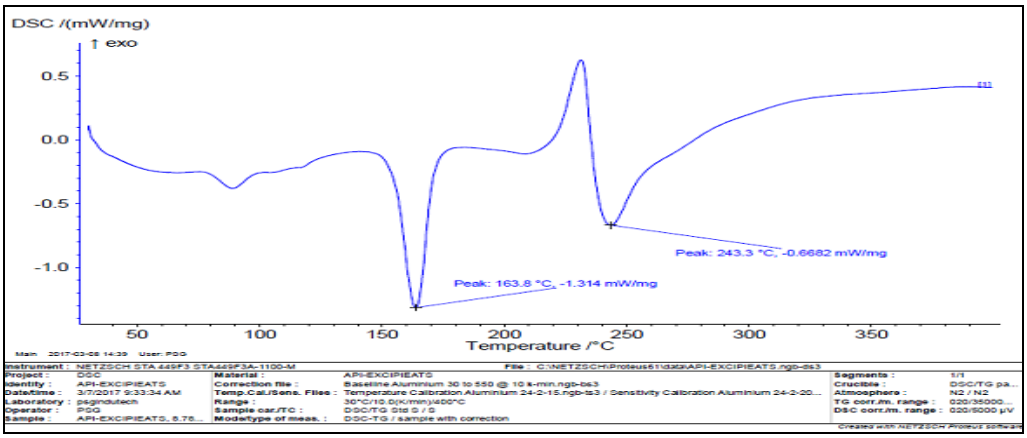

FIG. 3: DSC OF MDTs PREPARED BY DIRECT COMPRESSION METHOD

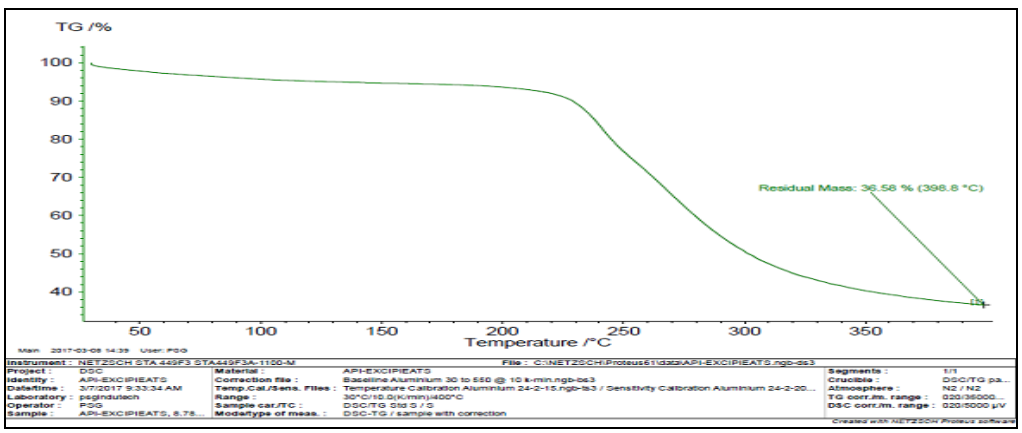

FIG. 4: TGA OF MDTs PREPARED BY DIRECT COMPRESSION METHOD

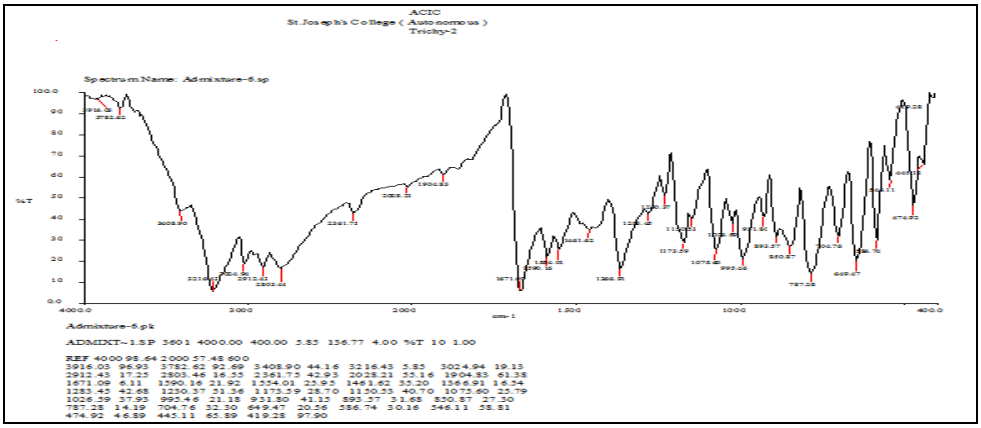

FIG. 5: FTIR SPECTRUM OF MDTs PREPARED BY SUBLIMATION METHOD

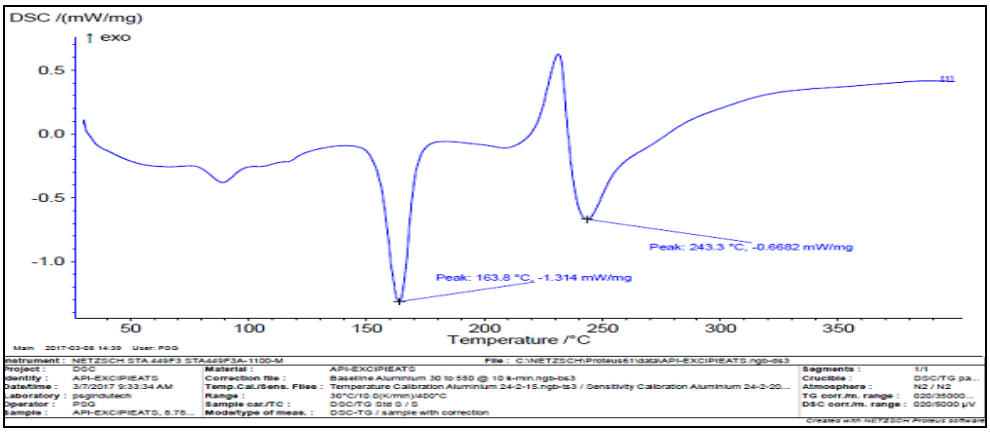

FIG. 6: DSC OF MDTs PREPARED BY SUBLIMATION METHOD

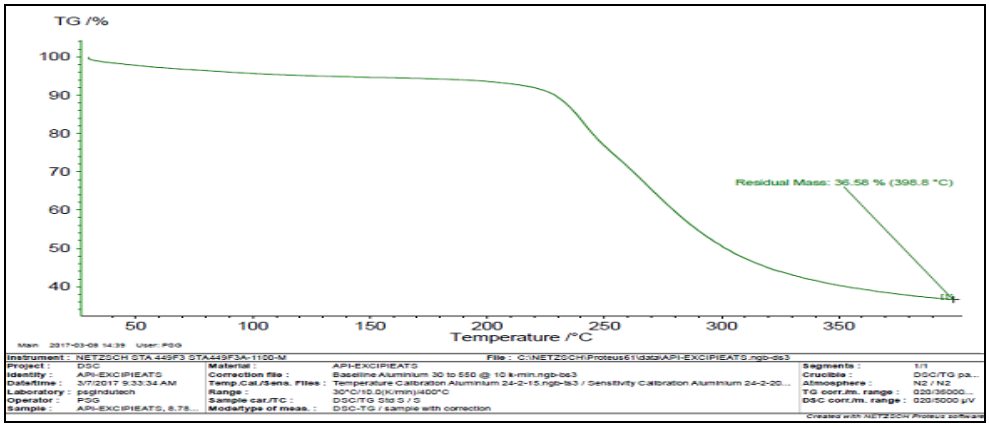

FIG. 7: TGA OF MDTs BY SUBLIMATION METHOD

Pre- Compression Studies:

TABLE 1: DIRECT COMPRESSION METHOD [20]

Batch code	Angle of repose (θ)	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Carr's Index (%)	Hausner's Ratio
API	24.76±0.18	0.31±0.06	0.34±0.08	08.82±0.07	1.09±0.02
F1	37.97±0.16	0.33±0.10	0.39±0.10	15.38±0.06	1.18±0.03
F2	36.02±0.26	0.31±0.10	0.42±0.08	26.19±0.09	1.19±0.02
F3	35.06±0.11	0.36±0.05	0.40±0.03	10.00±0.17	1.35±0.01
F4	34.09±0.13	0.34±0.06	0.43±0.01	21.95±0.68	1.18±0.02
F5	34.64±0.28	0.33±0.03	0.41±0.03	19.51±0.66	1.26±0.03
F6	26.06±0.26	0.32±0.05	0.39±0.03	17.94±0.42	1.17±0.01
F7	34.24±0.33	0.32±0.11	0.34±0.10	05.88±0.08	1.21±0.01
F8	36.96±0.31	0.34±0.10	0.38±0.11	10.52±0.04	1.11±0.02
F9	38.08±0.23	0.35±0.10	0.41±0.05	14.63±0.07	1.17±0.03

TABLE 2: SUBLIMATION METHOD [20]

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

TABLE 3: FORMULA FOR MOUTH DISSOLVING TABLETS OF HYDRALAZINE HYDROCHLORIDE BY DIRECT COMPRESSION METHOD [20]

S. no.	Ingredients	Formulation code (amount per tablet in mg)								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Hydralazine HCl	50	50	50	50	50	50	50	50	50
2	Croscarmellose sodium	8	10	12	-	-	-	-	-	-
3	Crospovidone	-	-	-	8	10	12	-	-	-
4	Sod. Starch glycolate	-	-	-	-	-	-	8	10	12
5	Aspartame	5	5	5	5	5	5	5	5	5
6	Mannitol	50	50	50	50	50	50	50	50	50
7	Magnesium Stearate	2	2	2	2	2	2	2	2	2
8	MCC	83	81	79	83	81	79	83	81	79
9	Talc	2	2	2	2	2	2	2	2	2

Total weight of tablet = 200 mg

TABLE 4: FORMULA FOR MOUTH DISSOLVING TABLETS OF HYDRALAZINE HYDROCHLORIDE BY SUBLIMATION METHOD [20]

S. no.	Ingredients	Formulation code (amount per tablet in mg)								
		SF1	SF2	SF3	SF4	SF5	SF6	SF7	SF8	SF9
1	Hydralazine HCl	50	50	50	50	50	50	50	50	50
2	Crospovidone	6	8	10	-	-	-	-	-	-
3	Croscarmellose sodium	-	-	-	6	8	10	-	-	-
4	Sod. Starch glycolate	-	-	-	-	-	-	6	8	10
5	Aspartame	5	5	5	5	5	5	5	5	5
6	Mannitol	50	50	50	50	50	50	50	50	50
7	Magnesium state	2	2	2	2	2	2	2	2	2
8	Camphor	2	4	6	2	4	6	2	4	6
9	MCC	83	80	77	83	80	77	83	80	77
10	Talc	2	2	2	2	2	2	2	2	2

Total weight of tablet = 200 mg

TABLE 5: EVALUATION OF HYDRALAZINE HYDROCHLORIDE MOUTH DISSOLVING TABLETS BY DIRECT COMPRESSION METHOD [20]

Parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9
Weight variation test (mg)	200±0.98	201±0.76	199±0.63	197±0.73	201±0.66	199±0.84	200±0.65	201±0.94	201±0.84
Thickness (mm)	2.9±0.02	2.8±0.01	3.0±0.02	3.1±0.04	3.5±0.03	3.7±0.02	2.4±0.08	2.5±0.02	2.8±0.09
Hardness test (kg/cm^3)	2.7±0.33	2.8±0.12	3.0±0.24	3.1±0.2 2	3.5±0.31	3.7±0.42	2.4±0.17	2.5±0.19	2.8±0.27
Friability (%)	0.56±0.17	0.42±0.22	0.51±0.25	0.29±0.17	0.53±0.23	0.56±0.27	0.72±0.19	0.77±0.14	0.79±0.21
Disintegration time (sec)	48±0.84	42±0.64	40±0.68	32±0.92	30±0.87	26±0.68	55±0.83	53±0.84	50±0.73
Wetting time (sec)	46±0.36	40±0.91	39±0.44	30±0.64	28±0.92	22±0.54	51±0.43	50±0.56	48±0.82
Water absorption (%)	71.41±0.73	70.43±0.61	74.98±0.47	84.32±0.65	88.32±0.94	92.87±0.91	64.32±0.43	65.42±0.74	68.50±0.53
Drug content (%)	92.16±0.36	94.68±0.24	97.14±0.42	97.01±0.44	98.42±0.67	99.98±0.56	88.48±0.37	90.50±0.25	91.80.52

TABLE 6: EVALUATION OF HYDRALAZINE HYDROCHLORIDE MOUTH DISSOLVING TABLETS BY SUBLIMATION METHOD [20]

	Formulation Code (Sublimation Method)								
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

TABLE 7: COMPARATIVE *IN-VITRO* DISSOLUTION STUDY OF MDTS PREPARED BY DIRECT COMPRESSION METHOD [20]

	Time (min)						
Formulation code	**0**	**2**	**4**	**6**	**8**	**10**	**12**
F1	2.27±0.65	11.29±0.59	30.13±0.64	51.27±0.82	60.13±0.84	76.52±0.58	91.80±0.45
F2	3.00±0.46	16.69±0.62	34.41±0.38	45.95±0.59	54.68±0.67	65.70±0.43	87.43±0.58
F3	5.61±0.54	18.40±0.36	31.66±0.45	45.68±0.78	54.90±0.58	76.85±0.63	92.86±0.39
F4	5.34±0.55	15.40±0.53	25.00±0.64	46.93±0.39	60.13±0.55	71.53±0.57	88.88±0.64
F5	7.80±0.37	17.91±0.71	37.50±0.59	49.71±0.52	64.99±0.73	76.52±0.80	94.30±0.61
F6	5.20±0.64	20.80±0.83	38.20±0.55	51.57±0.68	62.80±0.63	76.82±0.43	95.34±0.55
F7	5.75±0.81	18.57±0.45	32.61±0.58	45.68±0.85	64.82±0.52	72.98±0.55	85.25±0.43
F8	5.26±0.58	22.17±0.51	33.81±0.39	49.55±0.78	62.72±0.64	78.43±0.76	89.75±0.57
F9	4.39±0.57	21.98±0.67	36.84±0.54	49.55±0.66	72.68±0.63	79.30±0.82	95.59±0.64

TABLE 8: COMPARATIVE *IN-VITRO* DISSOLUTION STUDY OF MDTs PREPARED BY SUBLIMATION METHOD [20]

	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

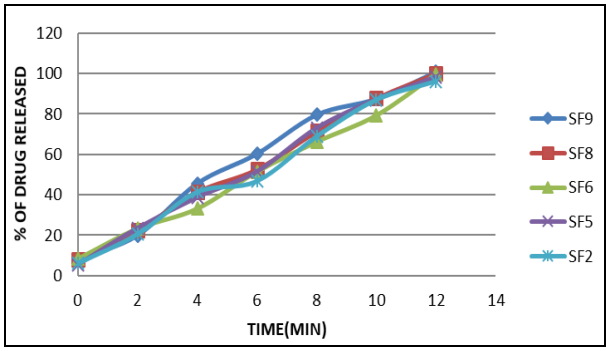

FIG. 9: COMPARATIVE *IN-VITRO* DISSOLUTION STUDY OF MDTs PREPARED BY SUBLIMATION

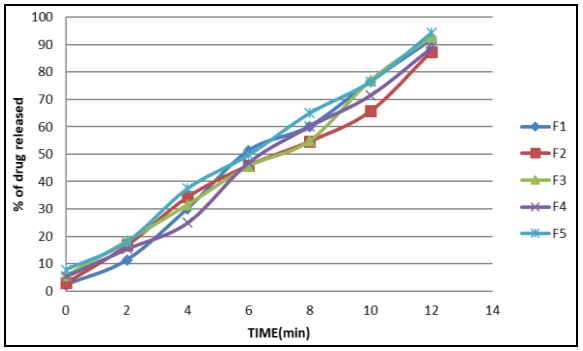

FIG. 8: COMPARATIVE *IN-VITRO* DISSOLUTION STUDY OF MDTs PREPARED BY DIRECT COMPRESSION METHOD [20]

DISCUSSION: Pre-compression Studies: The data obtained for pre-compressional parameters such as bulk density, tapped density, Hausner's ratio, Carr's index and angle of repose are shown in **Table 1**, **Table 2** and found within acceptable Pharmacopoeia standards.

Formulation and Development: Mouth dissolving tablets of Hydralazine Hydrochloride were prepared by direct compression method and sublimation method and the formulas were presented in **Table 3** and **Table 4**.

Post-compression Studies: Evaluations like weight variation, thickness, hardness, friability, wetting time, water absorption ratio assay, wetting time, *in vitro* disintegration time, *in vitro* drug dissolution study are mentioned in **Table 5, Table 6, Table 7, Table 8** and **Fig. 8, Fig. 9**. The weight variation test for the optimised formulation F9 and SF9 of mouth dissolving tablets prepared by both the methods were measured in the range of 201 ± 0.94 mg and 201 ± 0.34 mg, Thickness was in the range of 2.8 ± 0.09 mm and 3.02 ± 0.45 mm, hardness in the range of 2.8 ± 0.27 kg/cm^2 and 3.34 ± 0.47 kg/cm^2. The percentage friability was less than 1% for all formulations ensuring mechanical stability of the formulated tablets.

TABLE 9: STABILITY STUDY FOR OPTIMISED FORMULATION F9 PREPARED BY DIRECT COMPRESSION METHOD

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 color	White color	White color	White color	White color	White color	White color
2	Average weight (mg)	201	201	201	202	202	202	202
3	Friability (%)	0.26	0.26	0.28	0.29	0.27	0.26	0.31
4	Hardness (kg/cm^2)	3.7	2.6	2.6	2.5	2.6	2.6	2.5
5	Disintegration time (sec)	26	26	27	27	26	26	27
6	Drug content (%)	99.98	99.97	99.95	99.94	99.80	99.16	99.03

TABLE 10: COMPARATIVE *IN-VITRO* DISSOLUTION PROFILE OF ODTS OF HYDRALAZINE HCl (F9) PREPARED BY DIRECT COMPRESSION METHOD, BEFORE AND AFTER STORAGE AT 40 °C ± 2 °C AND 75% ± 5% RH

Time in minutes	Cumulative % of drug released (± 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	14.64 ± 1.25	14.68 ± 1.34	14.45 ± 1.22	14.34 ± 1.20	14.28 ± 5.42	13.55 ± 2.03	14.79 ± 5.26
4	44.05 ± 1.47	44.01 ± 2.17	43.98 ± 1.40	43.68 ± 1.31	43.31 ± 1.477	43.67 ± 2.60	44.66 ± 1.79
6	72.52 ± 0.65	72.50 ± 0.81	71.23 ± 0.44	72.01 ± 0.12	71.50 ± 0.61	72.33 ± 0.78	72.63± 0.97
8	83.29 ± 0.69	83.29 ± 0.67	82.18 ± 0.58	83.14 ± 0.24	82.86 ± 0.14	83.16 ± 0.62	82.44 ± 0.74
10	89.78 ± 0.58	89.70 ± 0.86	89.56 ± 0.72	89.10 ± 0.24	89.70 ± 0.13	89.84 ± 0.22	89.68 ± 0.52
12	90.20 ± 0.58	90.10 ± 0.24	90.01 ± 0.64	89.92 ± 0.82	89.65 ± 0.35	89.30 ± 0.12	89.42 ± 0.52

All formulations were evaluated for percentage drug content and found in the range of 92.16 ± 0.36 to 99.98 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.* 30.047 to 55.083 seconds indicating suitability of formulation for mouth dissolving tablet. Wetting time found in the range of 46±0.36 seconds and 50 ± 0.56 seconds, water absorption ratio was 65.42 ± 0.74 percentage and 71.41 ± 0.73 percentages. *In vitro* study was found to be optimum for the formulation F9 and SF9 in the range of 95.59 ± 0.64 percentages and 99.98 ± 0.77 percentages at 12 minutes. Stability results represented in **Table 9, Table 10** and **Fig. 10** also indicated that the optimised formulation F9 shows better stability under accelerated condition as per the Pharmacopoeia standards.

TABLE 11: STABILITY STUDY FOR OPTIMISED FORMULATION SF9 PREPARED BY SUBLIMATION METHOD [21]

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 color	White colour	White color	White color	White color	White color	White color
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 12: COMPARATIVE *IN-VITRO* DISSOLUTION PROFILE OF FAST DISSOLVING TABLETS OF HYDRALAZINE HYDROCHLORIDE (SF9) PREPARED BY SUBLIMATION METHOD, 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

Stability results represented in **Table 11, Table 12** and **Fig. 11** also indicated that the optimised formulation SF9 showed good results under accelerated condition as per the Pharmacopoeia standards.

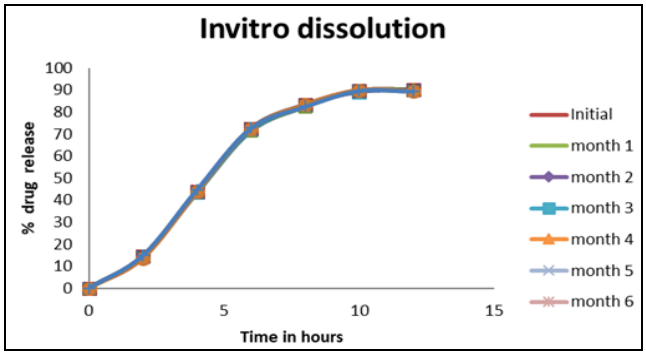

FIG. 10: COMPARATIVE *IN-VITRO* DISSOLUTION PROFILE OF ODTs OF HYDRALAZINE HCl (F9) PREPARED BY DIRECT COMPRESSION METHOD, BEFORE AND AFTER STORAGE AT 40 °C ± 2 °C TO 75% ± 5% RH

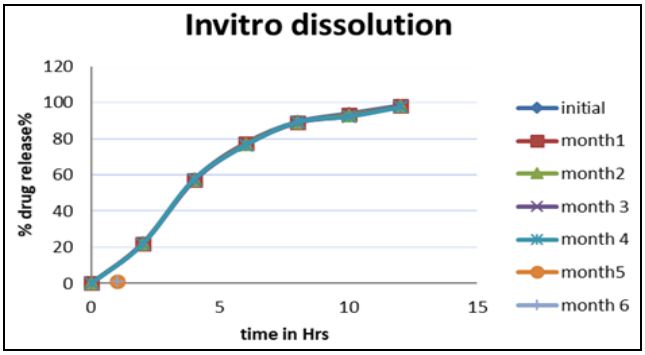

FIG. 11: COMPARATIVE *IN-VITRO* DISSOLUTION PROFILE OF ODTs OF HYDRALAZINE HCl (SF9) PREPARED BY SUBLIMATION METHOD, BEFORE AND AFTER STORAGE AT 40 °C ± 2 °C TO 75% ± 5% RH

CONCLUSION: From this study F9 and SF9 were 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.

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