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DESIGN AND EVALUATION OF HYDRALAZINE MOUTH DISSOLVING TABLET

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ABSTRACT
Hydralazine is the first-line therapy for hypertension in pregnancy. Hydralazine is used to treat severe hypertension, but it is not a first-line therapy for essential hypertension. Tablet dosage form is the most popular among all existing conventional dosage forms because of its convenience of self administration, compactness and easy manufacturing. Many patients find it difficult to swallow tablets and capsules.Mouth Dissolving Tablets is a solid dosage form that dissolves or disintegrates within a minute in the oral cavity without the need of water and has a pleasant taste. MDT is also known as orally disintegrating tablet, fast-dissolving tablet, fast-melting tablet, mouth melting tablet or fast-disintegrating tablet.The formulas were evaluated for compatibility and Precompressional studies. The formulations were evaluated for weight variation, thickness, hardness, friability, content uniformity, disintegration time, wetting time, water absorption ratio and release profile.

KEY WORDS- *Hydralazine, Hypertension, Mouth Dissolving Tablet,orally disintegrating tablet, Precompressional studies, disintegration time.*

INTRODUCTION

Tablet dosage form is the most popular among all existing conventional dosage forms because ofits convenience of self administration, compactness and easy manufacturing. Many patients findit difficult to swallow tablets and capsules. The difficulty is experienced in particular by pediatricand geriatric patients, but it also applies to people who are ill on bed and to those active working patients who are busy or traveling, especially those who have no access to water.

Mouth Dissolving Tablets are designed to disintegrate or dissolve rapidly on contact with saliva, thus eliminating theneed for chewing the tablet, swallowing an intact tablet, or taking the tablet with water. Althoughno water is needed to allow the drug to disperse quickly and efficiently, most technologies utilizethe body's own salivation. This mode of administration was initially expected to be beneficial to pediatric and geriatric patients, to people with conditions related to impair swallowing, and for treatment of patients when compliance may be difficult.

Hydralazine is the first-line therapy for hypertension in pregnancy, with methyldopa. Hydralazine is used to treat severe hypertension, but it is not a first-line therapy for essential hypertension. Hydralazine is not used as a primary drug for treating hypertension because it elicits a reflex sympathetic stimulation of the heart (the baroreceptor reflex). The sympathetic stimulationmay increase heart rate and cardiac output, and in patients with coronary artery disease may cause angina pectoris or myocardial infarction. Hydralazine may also increase plasma renin concentration, resulting in fluid retention. In order to prevent these undesirable side-effects, hydralazine is usually prescribed in combination with a beta-blocker (e.g. propranolol) and a diuretic.

MATERIALS AND METHODS

The drug Hydralazine Hydrochloride was obtained from GlaxoSmithKline Pharmaceuticals Ltd., Mumbai. Ac- di- sol,Lactopress, Micro crystalline cellulose (MCC), Sodium starch glycolate (SSG) was obtained from Qualigens® fine chemicals, Navi Mumbai. Crospovidone from ACS chemicals. Dihydrogen ortho phosphate from Rankem (New Delhi). Ethanol, Hydrochloric acid, Methanol, Sodium hydroxide was obtained from Himedia, media india. and Dextrose and Talc from Central Drug House(P) Ltd., New Delhi and all other excipient used were analytical grade.

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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.

Formulation and Development

Precompressional studies

Precompressional parameters like bulk density, tapped density, compressibility index and hausner ratio, Angle of Repose and Determination of *in-vitro* Drug Release resinate was performed as per the standard procedures.

Preparation of Hydralazine Mouth Dissolving Tablet by Using Superdisintegrants

The critical parameters to formulate a mouth dissolving tablet are the choice of superdisintegrant and optimization of concentration of superdisintegrant. The main criterion for mouth dissolving tablets is to disintegrate or dissolve rapidly in the oral cavity within 15 seconds to 1 minute. The mouth dissolving tablets of hydralazine were prepared by using superdisintegrants in different ratios. The ingredients were mixed homogenously and co-grounded in a glass mortar and pestle (except talc and magnesium stearate). Finally talc and magnesium stearate were added and mixedfor 5 minutes. The mixed blends of hydralazine with other excipients were compressed using single punch tablet machine.

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 also specific tests for the evaluation of mouth dissolving tablets like wetting time and water absorption ratio were performed. In vitro drug release profile were fitted with various kinetic equations like Higuchi, Hixson and Crowell model and Korsmeyer and Peppas equation to understand the drug release kinetics from the dosage form.

Results: Hydralazine hydrochloride appeared white, odourless, amorphous, and soluble in water with a melting point of 273 ± 0.1 °C.

Determination of *in-vitro* Drug Release from Resinate

Table no. 1: *in-vitro* Dissolution of Drug Release in pH 1.2, 6.8, 7.4

Time (min)	% Drug Release from Resinate		
	pH 1.2	pH 6.8	pH 7.4
0	0	0	0
5	12.03	9.90	2.24
10	21.68	18.48	5.65
15	30.32	24.97	8.88
20	40.08	31.50	11.06
30	49.88	43.39	12.19

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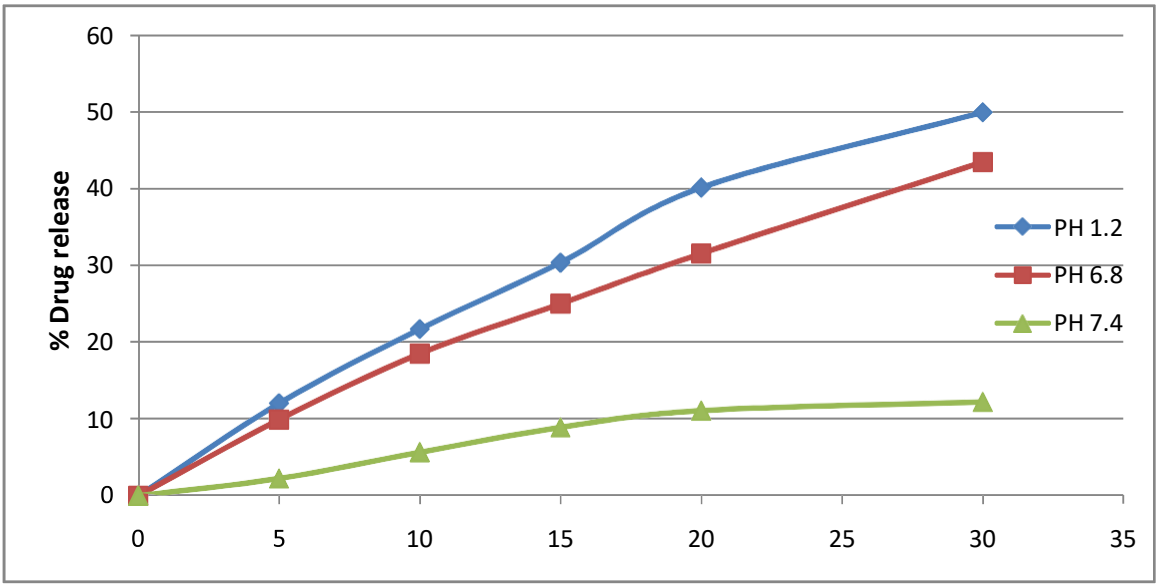

Figure no. 1: *in-vitro* Dissolution of Drug Release in pH (a) 1.2 □, (b) 7.4 ▲, (c) 6.8■

Table 2: Preparation of Hydralazine HCl Mouth Dissolving Tablet Hydralazine HCl Mouth Dissolving Tablet preparation by Using SuperdisintegrantsTable no. 3: Formulation of Mouth Dissolving Tablets with Resinate

Ingredients	FDT1	FDT2	FDT3	FDT4	FDT5	FDT6
Drug resinates equivalent to 5 mg of hydralazine HCl	35 mg	35 mg	35 mg	35 mg	35 mg	35 mg
Crospovidone	3 mg	4 mg	-	-	-	-
Ac-Di-Sol	-	-	3 mg	4 mg	-	-
SSG	-	-	-	-	3 mg	4 mg
MCC	26	26	26	26	26	26
Dextrose	15	15	15	15	15	15
Lactopress	15	15	15	15	15	15
Talc	2	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2	2

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Evaluation of Tablet Blend

Table no. 3: Evaluation of Tablet Blend

Ingredients	FDT1	FDT2	FDT3	FDT4	FDT5	FDT6
Bulk Density (gm/cm^3)	0.584± 0.009	0.625± 0.007	0.611± 0.006	0.627± 0.006	0.633± 0.005	0.574± 0.012
Tapped Density (gm/cm^3)	0.666± 0.007	0.718± 0.008	0.711± 0.010	0.714± 0.011	0.715± 0.011	0.649± 0.003
Compressibilty Index (%)	12.212± 0.005	12.952± 0.005	14.051± 0.010	12.220± 0.004	11.447± 0.015	11.499± 0.004
Hausners Ratio	1.126± 0.392	1.134± 0.544	1.136± 0.765	1.112± 0.795	1.129± 1.233	1.117± 0.782
Angle of Repose	22.713± 0.953	22.931± 0.268	23.189± 0.553	23.756± 0.434	23.282± 0.754	24.231± 0.725

Characterization of Mouth Dissolving Tablets

Table no. 4: Characterization of Mouth Dissolving Tablets

Ingredients	FDT1	FDT2	FDT3	FDT4	FDT5	FDT6
Thickness(mm)	2.313± 0.022	2.076± 0.121	2.329± 0.089	2.415± 0.025	2.361± 0.061	2.295± 0.066
Weight (mg)	99.133± 0.665	98.466± 0.737	99.4± 0.264	100.833± 1.450	97.233± 0.602	97.733± 0.321
Hardness (kg/cm^3)	2.713± 0.156	2.913± 0.200	3.043± 0.150	3.003± 0.090	2.800± 0.191	2.990± 0.101
Friability (%)	0.823± 0.051	0.64± 0.05	0.536± 0.030	0.626± 0.045	0.653± 0.081	0.856± 0.041
in-vitro Disintegration time(s)	51.66± 2.51	20.66± 2.08	62.66± 2.516	38.00± 3.00	66.33± 3.05	41.66± 1.52
Wetting time (s)	47.33± 6.02	18.66± 2.51	57.66± 3.51	32.33± 3.51	55.66± 6.11	38.33± 2.08
in vitro Dispersion Time (s)	57.33± 1.52	26.33± 2.08	63.63± 2.08	31.33± 2.51	68.66± 2.08	46.00± 2.64

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Content Uniformity

Table no. 5: Drug Content in the Mouth Dissolving Tablet of Hydralazine HCl

Formulations Code	Parameters	
	Drug Content (mg per Tablet)	Drug Content (%)
FDT1	4.86±0.25	97.2
FDT2	4.93±0.35	98.7
FDT3	4.83±0.30	96.7
FDT4	4.96±0.42	99.2
FDT5	4.94±0.25	98.8
FDT6	4.97±0.31	99.4

***In-Vitro* Dissolution Studies**

Table no. 6: *In-Vitro* Release Data of Hydralazine HCl Tablet

Time (min.)	Cumulative Percent Drug Released					
	FDT1	FDT2	FDT3	FDT4	FDT5	FDT6
0.000	0.000	0.000	0.000	0.00	0.000	0.000
1.000	74.27	77.58	68.75	70.96	57.72	61.03
2.000	77.99	84.63	70.33	74.22	64.66	67.99
3.000	85.04	89.51	72.98	76.89	69.43	73.88
4.000	92.13	95.52	80.73	85.66	73.12	78.70
5.000	94.84	98.25	81.67	90.54	75.72	80.23

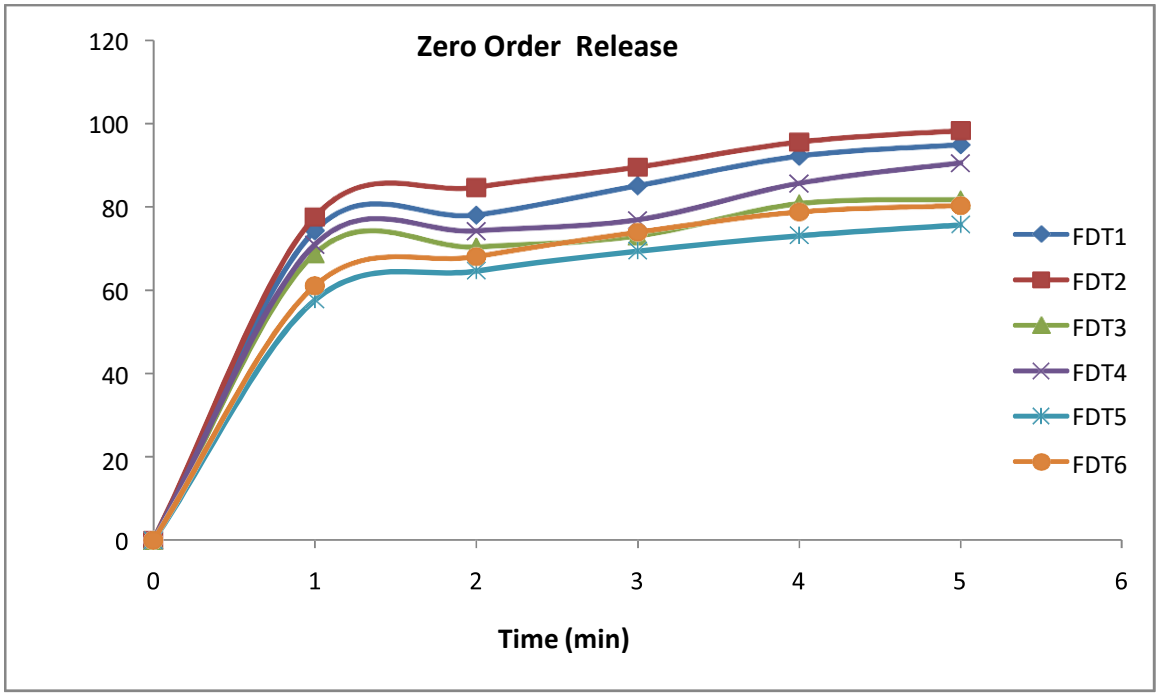

Figure no. 2: *in-vitro* Release curve of Hydralazine HCl Tablet-Zero Order Release

Log % Drug Retained Data of Hydralazine HCl Tablet

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Table no. 7: *in-vitro* Log % Drug Retained Data of Hydralazine HCl Tablet

Time (min.)	Log Cumulative Percent Drug Retained					
	FDT1	FDT2	FDT3	FDT4	FDT5	FDT6
0	2	2	2	2	2	2
1	1.410	1.350	1.494	1.462	1.626	1.590
2	1.342	1.186	1.472	1.411	1.548	1.505
3	1.174	1.020	1.431	1.363	1.485	1.416
4	0.895	0.651	1.284	1.156	1.429	1.328
5	0.712	0.243	1.263	0.975	1.385	1.296

Comparision of Release with Marketed Tablets

Table no. 8: *in-vitro* Release Profile of Hydralazine HCl Marketed Tablets

Time (min)	Cumulative % Drug Release (Marketed)	Log Cumulative %Drug Retained (Marketed)
0	0	2
1	9.53	1.95
2	18.46	1.91
3	24.64	1.88
4	28.74	1.85
5	38.33	1.79
30	43.73	1.75
60	46.37	1.73

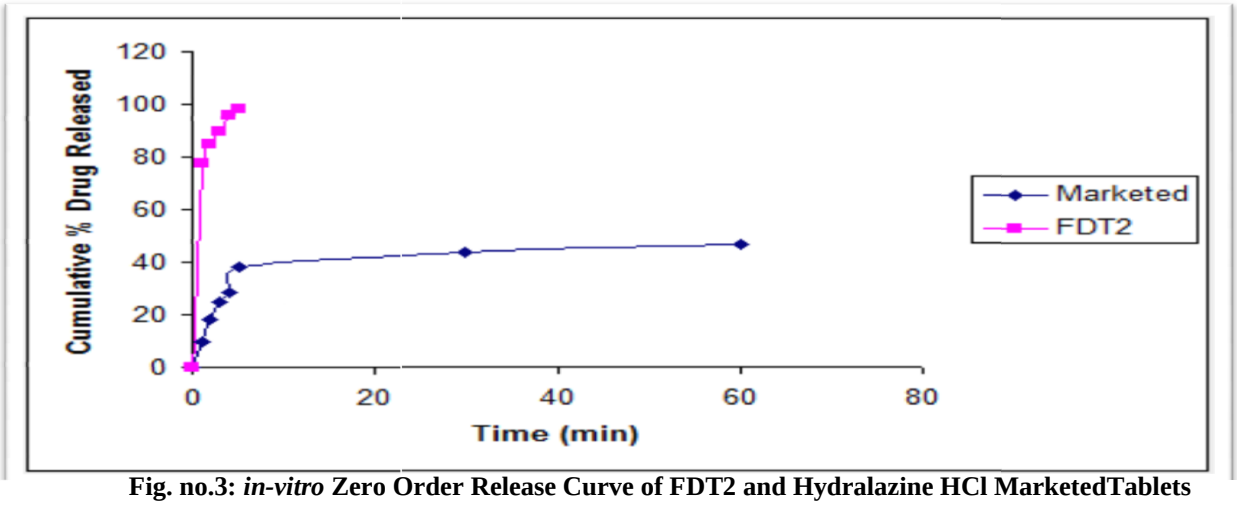

Fig. no.3: *in-vitro* Zero Order Release Curve of FDT2 and Hydralazine HCl MarketedTablets

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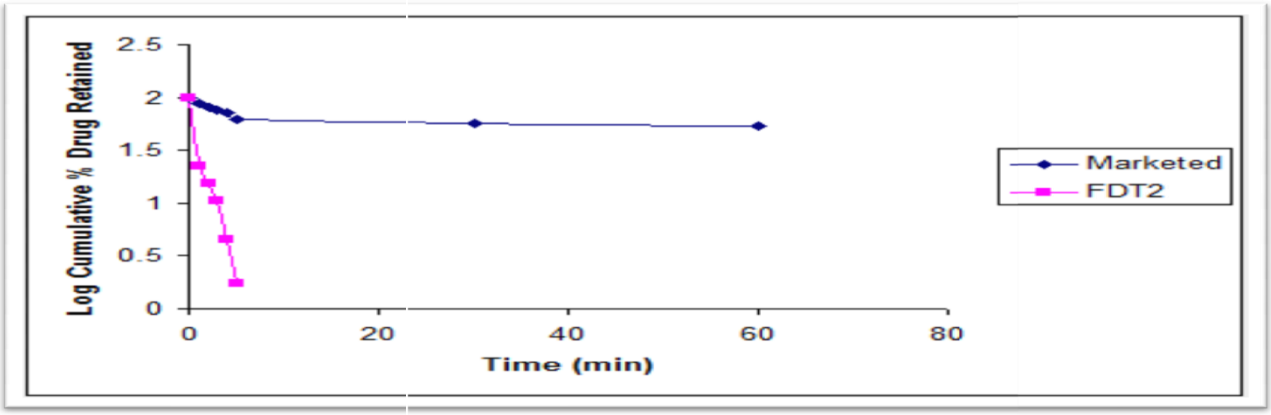

Fig. no. 4: *in-vitro* First Order Release Curve of FDT2 and hydralazine HCl Marketed Tablets

DISCUSSION

In this study, novel mouth dissolving taste masked tablets of hydralazine HCl with adequate mechanical strength were prepared, optimized and evaluated for various *in-vitro* and *in-vivo* parameters.

The obtained sample of hydralazine HCl was identified by various organoleptic, physicochemical and spectrophotometeric methods. The sample of hydralazine HCl posses similar color, odor, taste and texture as given in officials.

The drug content of all formulations was determined spectrophotometrically at 220 nm. It varied from 4.86 ± 0.25 to 4.97 ± 0.35 mg per tablet. The uniformity of drug content was also shownthe uniformity of tablet punching process.*in-vitro* drug release experiments were performed at 37±0.5ºC in paddle type dissolution apparatus. The results showed that all the formulations release the drug within 6 to 7 minutes.The maximum drug release was found in formulation FDT2 (98.747%).
The order of drug release was found to be:
FDT2 >FDT1 >FDT4 >FDT3 >FDT6 >FDT5

CONCLUSION

In the present study mouth dissolving tablets of hydralazine HCl were designed, prepared and evaluated. These tablets can disintegrate or dissolve rapidly once placed into the oral cavity. The feofenadine was analyzed for its organoleptic, physicochemical and spectral (IR, UV) properties.The disintegration properties of tablet were observed as Crospovidone > Ac-Di-Sol > Sodium starch glycolate**.** On applying zero order and first order dissolution kinetic treatments, it was found that all the prepared tablets followed first order kinetics.

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