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Development and characterization of hydralazine mouth dissolving tablet

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***Abstract*---**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. The difficulty is experienced in particular by pediatric and 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. The drug hydralazine HCl were used. The amount of drug was 35 mg. the different super disintegrates was used to make a suitable mouth dissolving tablet. All the other reagents which is used in analytical grade reagents. 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 obtained hydralazine HCl was concordant with reference specifications. A complex of hydralazine HCl was successfully formulated. The volunteers rated the resinate as tasteless and agreeable complex. The rapid drug dissolution might be due to the easy and fast breakdown of tablet and rapid absorption of drug into the dissolution media.

***Keywords*---**Hydralazine, Resinate, Disintegration, Dissolution.

1. Introduction

Mouth dissolving tablets dosage form is the most popular among all existing conventional dosage forms because of its convenience of self-administration, compactness and easy manufacturing.[1] Many patients find it difficult to swallow tablets and capsules. The difficulty is experienced in particular by pediatric and 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.[2] It s a novel dosage form which is placed in mouth and they rapidly dissolves and disintegrated in saliva within a few seconds .it take hardly 15 sec to 3 minutes [5,6]

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, 2,4]. 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.[7,8]

2. Materials and Methods

The drug hydralazine HCl were used the amount of drug was 35 mg. the different super disintegrates was used to make a suitable mouth dissolving tablet. All the other reagents which is used in analytical grade reagents.

2.1 Formulation methods

Table no 1 :- Hydralazine HCl Mouth Dissolving Tablet preparation

Ingredients	FDT1	FDT2	FDT3	FDT4	FDT5	FDT6
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

3. Results and Discussion

3.1. Physical properties of pure Hydralazine

Table no. 2: Table of drug (Hydralazine) properties

S. No.	Properties	Properties reported	Properties observed
01	Color	Yellow	Light Yellow
02	Odor	Odorless	Odorless
03	Taste	Bitter	Bitter
04	Physical State	Crystalline powder	Crystalline powder
05	Melting Point	273 ^{0}C	270 ^{0}C

3.2 Determination of solubility

Table no. 3: Solubility determination

S. no.	Solvents	Solubility observed
1	Ethanol	Freely soluble
2	Water	Soluble
3	0.1N HCl	Soluble
4	0.1N NaOH	Soluble
5	Methanol	Freely soluble

3.3 Scanning for Ultraviolet Absorption Maxima (λmax)

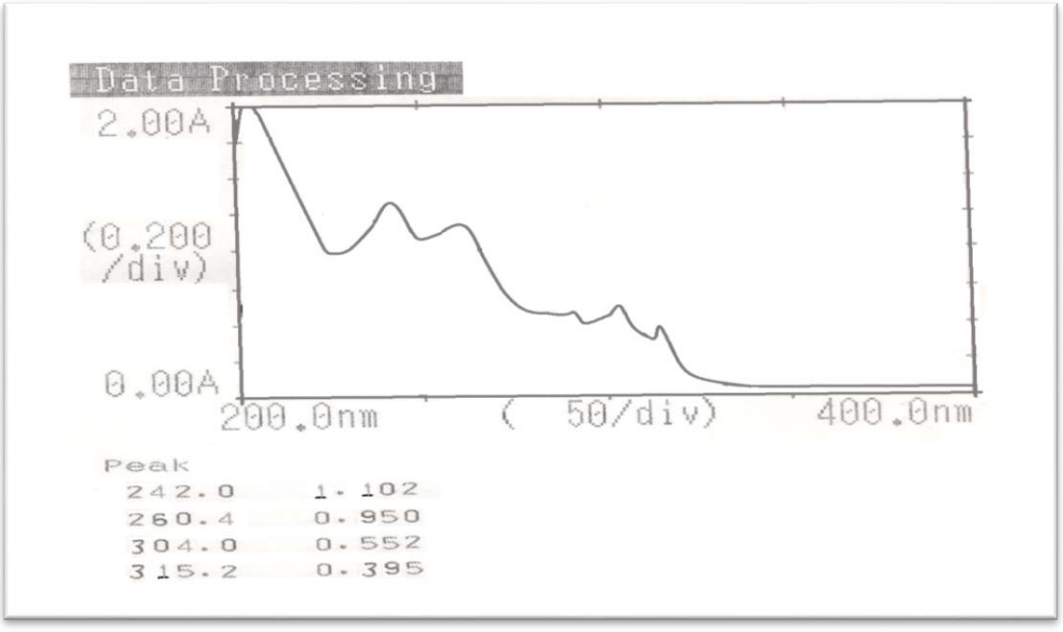

Figure no. 1: Scanning for ultraviolet absorption maxima

3.4 Drug Polymer Interaction Studies

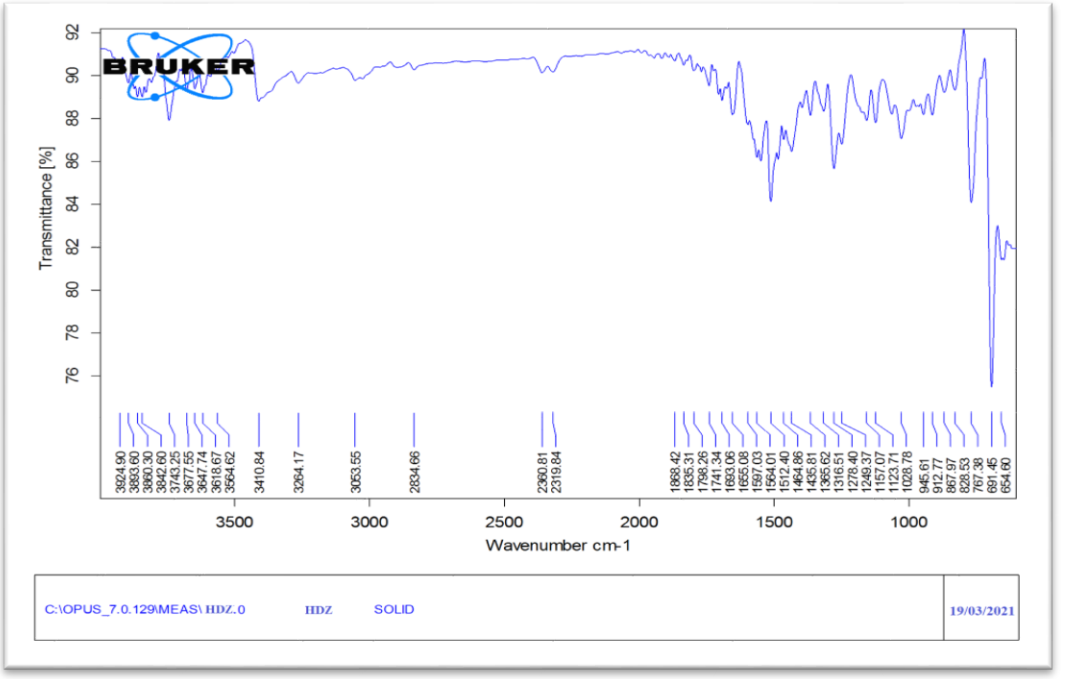

Figure no. 2: FT-IR spectrum of Hydralazine HCl

3.5 Preformulation Study

3.5. 1 Preparation of calibration curve

Table no. 4: Calibration curve data of Hydralazine HCl

S. No.	Concentration (µg/ml)	Absorbance
1.	0	0
2.	2	0.094
3.	4	0.184
4.	6	0.278
5.	8	0.362
6.	10	0.452

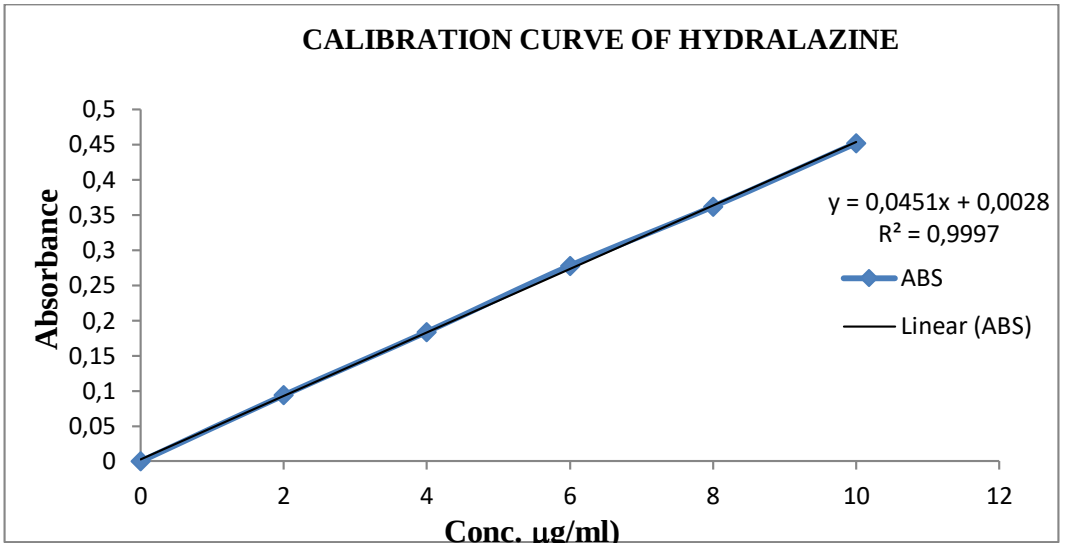

Figure no. 3: Calibration curve of Hydralazine HCl

3.5.2 Drug Polymer Interaction Studies

Table no. 4: Drug-Polymer Interaction Studies

Mixtures	Physical Change			IR Peak
	Liquefaction	Clumping	Color Change	
Drug	-	-	-	1637 1505 1134
Drug + Ac-di-sol	-	-	-	1636 1504 1133
Drug+crospovidone	-	-	-	1637 1499 1135
Resinate	-	-	-	1636 1505 1134

3.5.3 Effect of Various Parameters on Drug-Resin Adsorption

Table no. 5: Effect of Concentration of Resin on Drug Loading

D:R	Absorbance	Drug Percentage
1:1	0.281	33.42
1:2	0.203	36
1:3	0.176	39.98
1:4	0.141	40.87

3.5.4. Effect of Swelling by Stirring Speed and Time

Table no. 6: Effect of Swelling by Stirring Speed and Time

Time (min)	50 rpm		100 rpm	
	Absorbance	%Drug Loading	Absorbance	%Drug Loading
15	0.118	26.92	0.120	27.34
30	0.128	29.04	0.176	31.84

Table no. 7: Effect of Complexation Time on Drug Loading

Time (h)	Absorbance	% Drug Loading
1	0.102	23.16
2	0.118	26.89
3	0.153	34.62
4	0.190	43.21
5	0.194	43.92

Table no. 8: Effect of pH on Drug Loading

pH	1 h		2 h		3 h		4 h	
	Abs	% Drug loading	Abs	% Drug loading	Abs	% Drug loading	Abs	%Drug loading
1.2	0.394	6.81	0.519	11.76	0.765	17.33	0.839	19
6.8	0.172	39.05	0.199	45.14	0.212	48.10	0.251	57
7.4	0.150	33.47	0.165	39.13	0.180	42.81	0.186	44.12

3.5.5 in-vivo Taste Evaluation

Table no. 9: *in-vivo* Taste Evaluation

Volunteer	Taste Evaluation		
	Drug	Granules	Resinate
1	4	2	0
2	4	3	0
3	4	1	0
4	4	1	0
5	4	2	0
6	3	2	0

0: no bitterness, 1: threshold bitterness, 2: bitter, 3: moderate bitterness 4: strong bitterness

3.5.6 Physical Evaluation of granules

Table no. 10: Physical Evaluation of Resinate and Granules

Parameters	Resinate	Granules
Bulk Density (gm/cm^3)	0.611	0.628
Tapped Density (gm/cm^3)	0.702	0.694
Compressibilty Index (%)	12.962	9.523
Hausners Ratio	1.148	1.105
Angle of Repose	23.64	21.817

3.5.7 Determination of *in-vitro* Drug Release from Resinate

Table no. 11: *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

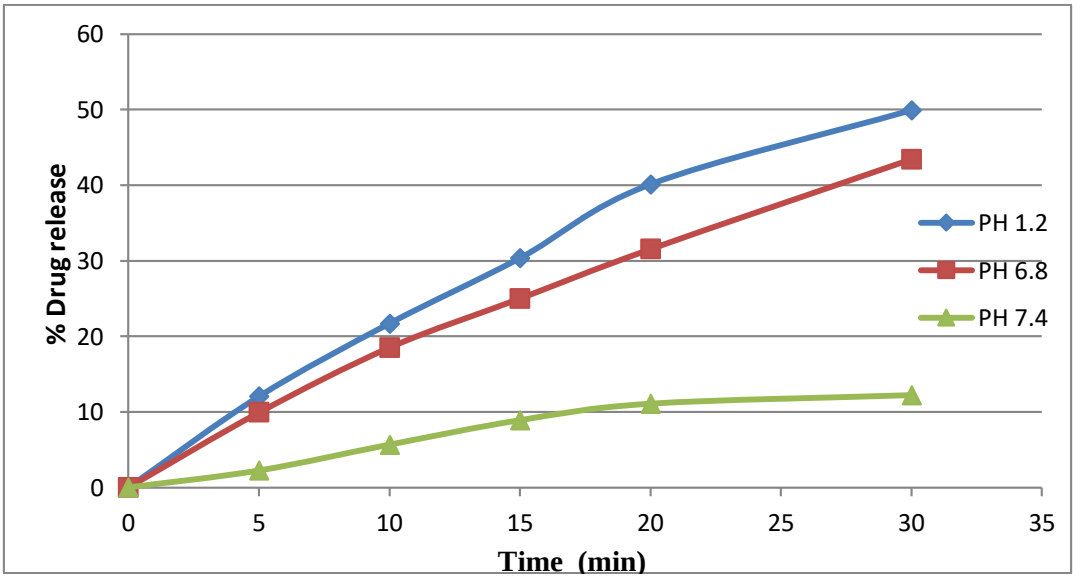

Figure no. 4 *in-vitro* Dissolution of Drug Release in pH (a) 1.2 •, (b) 7.4 ▲, (c) 6.8■

3.6 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

3.6.1 Content Uniformity

Table no. 15: 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

3.6.2 in-vitro Dissolution Studies

Table no. 16: *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

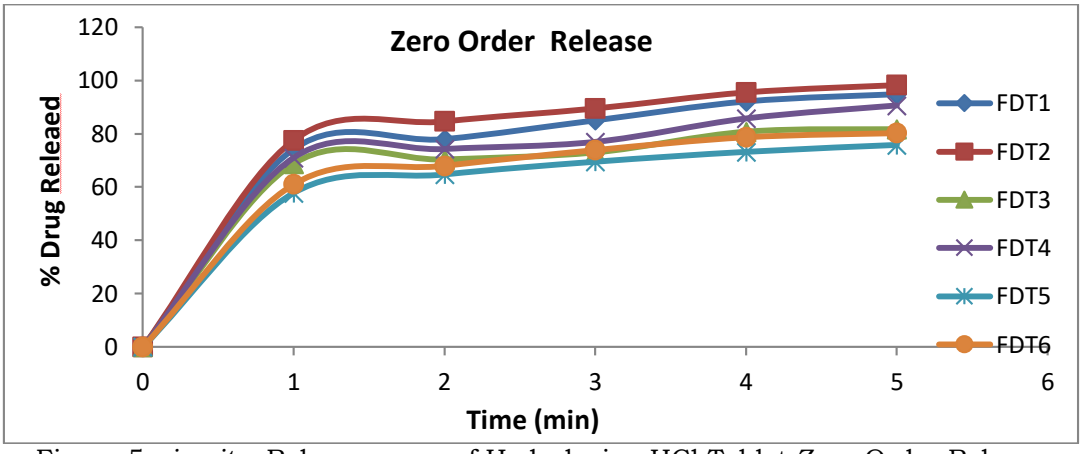

Figure 5 : *in-vitro* Release curve of Hydralazine HCl Tablet-Zero Order Release

3.6.3 Log % Drug Retained Data of Hydralazine HCl Tablet

Table no. 17: *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

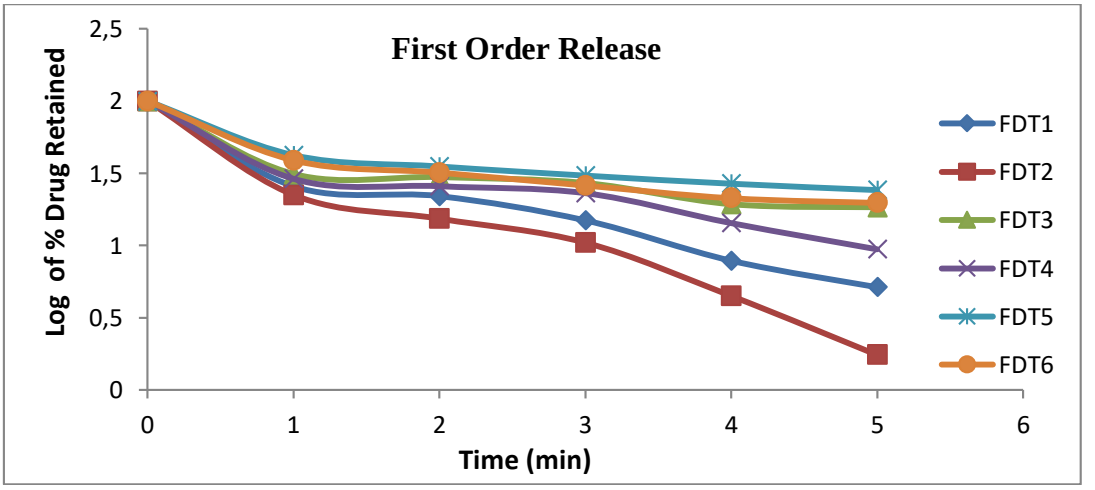

Figure no 6: *in-vitro* Drug Retained Curve of Hydralazine HCl Tablet-First Order Release

4. 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 obtained hydralazine HCl was concordant with reference specifications. A complex of hydralazine HCl was successfully formulated. The volunteers rated the resinate as tasteless and agreeable complex. 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.
The drug release was found as

FDT2 >FDT1 >FDT4 >FDT3 >FDT6 >FDT5

The rapid drug dissolution might be due to the easy and fast breakdown of tablet and rapid absorption of drug into the dissolution media.

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