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Formulation and *In-vitro* Evaluation of Dofetilide Fast Dissoloving Tablets

Narayana Rao Alla*, Usha Tatikonda, Dr. Satya Narayana Tanuku

Mother Theresa Pharmacy College, Sathupally, Khammam, Telangana, India

A B S T R A C T

The present study was aimed to formulate fast dissolving tablets of Dofetilide. In the present work Sodium starch glycollate, Cross povidone and Cross carmellose sodium were employed as super disintegrating agents to enhance the solubility and dissolution rate of selected drug molecule. All the formulations were prepared by direct compression method using 6mm punch on 8 station rotary tablet punching machine. The blend of all the formulations showed good flow properties such as angle of repose, bulk density, tapped density. The prepared tablets were shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations F4 formulation showed maximum % drug release i.e., 98.16 % in 30 min hence it is considered as optimized formulation. The F4 formulation contains Cross povidone as super disintegrate in the concentration of 5 mg.

Keywords: Dofetilide, Oro dispersible tablets, Super disintegrating agents, Direct compression

A R T I C L E I N F O

Corresponding Author
Narayana Rao Alla
Mother Theresa Pharmacy College,
Khothuru, Sathupally, Khammam
Telangana, India- 507303
MS-ID: JPBMAL3518

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C O N T E N T S

1. Introduction

Fast dissolving tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva. The faster the drug into solution, quicker the absorption and onset of clinical effect. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablets dosage form. The target of these new oral dissolving/disintegrating dosage forms have generally been pediatric, geriatric, bedridden and developmentally disabled patients and also patients with persistent nausea, who are in traveling, or who

have little or no access to water are also good candidates for ODTs.

The major advantage of the ODT formulation is that it combines the advantages of both liquid and conventional tablet formulations, and also offering advantages over both traditional dosage forms. It provides the convenience of a tablet formulation, and also allowing the ease of swallowing provided by the liquid formulation. ODTs allow the luxury of much more accurate dosing than primary alternate, oral liquid.

2. Materials and Methods

Dofetilide, Microcrystalline cellulose, Sodium starch glycollate, Cross povidone, Crooscarmellose sodium, Magnesium stearate, Talcchemicals were Laboratory grade made of SD Fine chemicals Pvt Ltd

Formulation of fast dissolving tablets of Dofetilide:

Preparation of tablets:

Composition of Dofetilide fast dissolving Tablet by direct compression. All the ingredients were weighed. Required quantity of drug and exciepients mixed thoroughly in a poly bag. The blend is compressed using rotary tablet machine-8 station with 6mm flat punch, B tooling. Each tablet contains 15 mg Dofetilide and other pharmaceutical ingredients. Total weight of tablet was found to be 100 mg.

Evaluation of post compression parameters for prepared Tablets:

The designed compression tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

3. Results and Discussion

Standard Calibration curve of Dofetilide:

It was found that the estimation of Dofetilide by UV spectrophotometric method at λ_{max}242nm in pH 6.8 Phosphate buffer had good reproducibility and this method was used in the study. The correlation coefficient for the standard curve was found to be closer to 1, at the concentration range, 2- 10µg/ml.

The regression equation generated was y = 0.050x + 0.004, R^2 = 0.999.

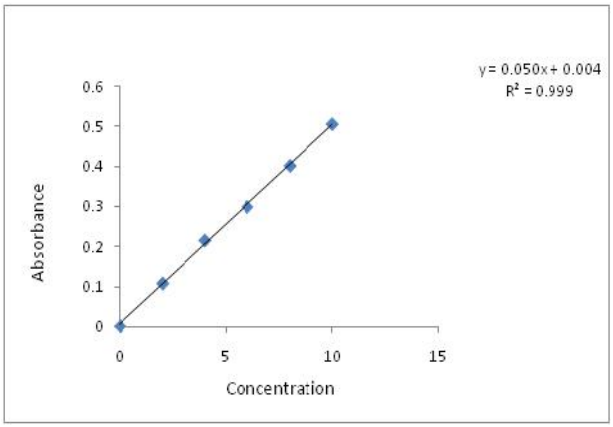

Figure 1: Standard graph of Dofetilide in pH 6.8 Phosphate buffer

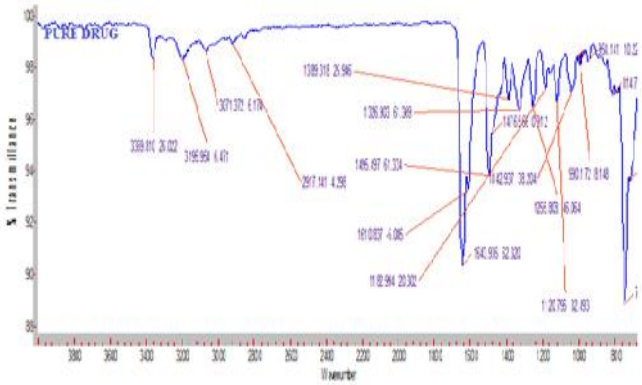

Figure 2: FT-IR spectrum of pure drug.

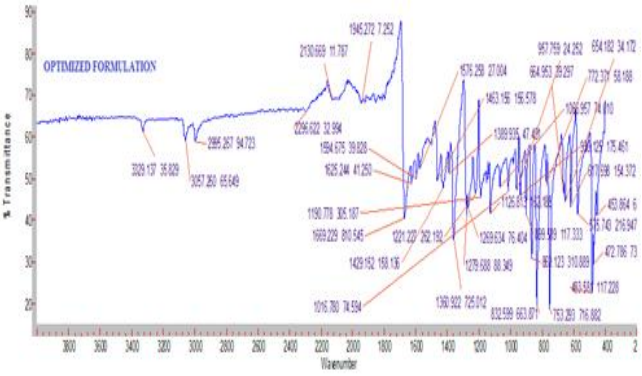

Figure 3: FT-IR spectrum of optimized formulation.

Evaluation Parameters for Fast Dissolving Tablets of Dofetilide:

Pre-compression parameters:

The data's were shown in Table 4,the values for angle of repose were found in the range of 26°-30°. Bulk densities and tapped densities of various formulations were found to be in the range of 0.41 to 0.50 (gm/cm^2) and 0.50 to 0.58 (gm/cm^2) respectively. Carr's index of the prepared blends fall in the range of 13.79% to 18.18%.The Hausner's ration fall in range of 1.6 to 1.22. From the result it was concluded that the powder blends had good flow properties and these can be used for tablet manufacture.

In-vitro Dissolution studies:

In-vitro dissolution studies were carried out by using 500ml of pH 6.8 Phosphate buffer in USP dissolution apparatus by using paddle method. The dissolution studies were carried out for about 30 min. The data were shown in the table no 6.

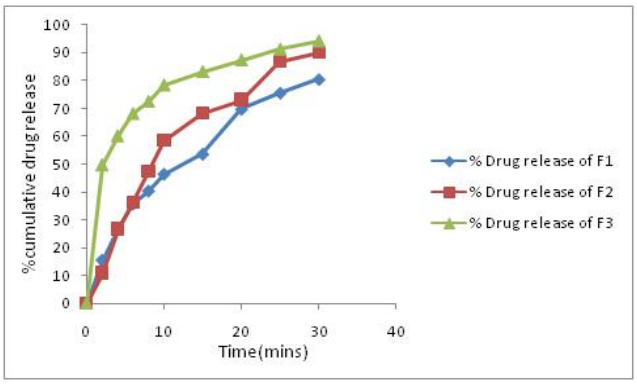

Figure 4: Dissolution profile of formulationsF1,F2,F3

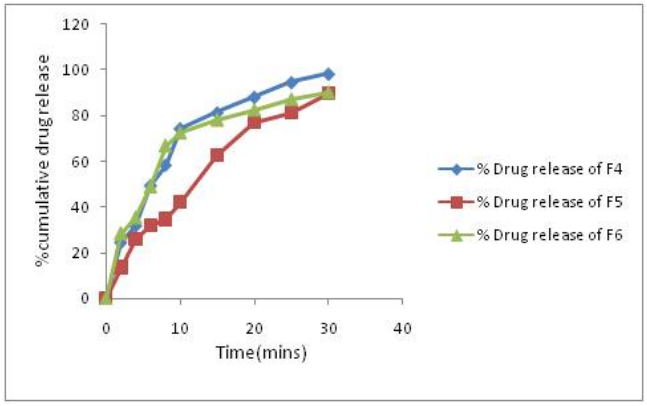

Figure 5: Dissolution profile of formulations F4, F5, F6

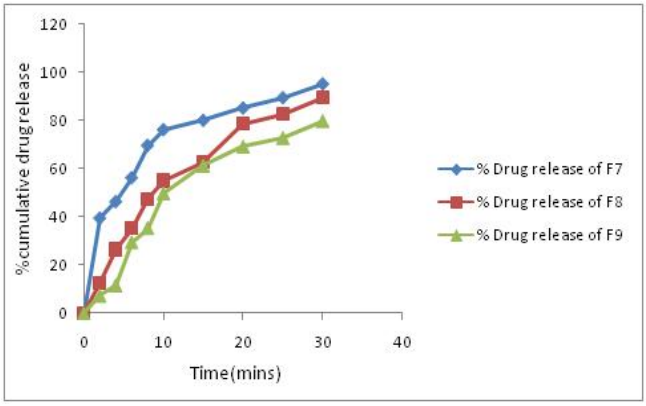

Figure 6: Dissolution profile of formulations F7,F8,F9

Table 1: Composition of various tablet formulations

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Dofetilide (mg)	15	15	15	15	15	15	15	15	15
SSG (mg)	5	10	15	---	---	---	---	---	---
Cross Povidone (mg)	---	---	---	5	10	15	---	---	---
Cross Carmellose Sodium (mg)	---	---	---	---	---	---	5	10	15
Magnesium Stearate(mg)	3	3	3	3	3	3	3	3	3
Talc(mg)	3	3	3	3	3	3	3	3	3
MCC(mg)	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs
Total wt(mg)	100	100	100	100	100	100	100	100	100

Table 2: Concentration and absorbance obtained for calibration curve of Dofetilide in pH 6.8 Phosphate buffer

S. No.	Concentration (µg/ml)	Absorbance* (at 242 nm)
1	2	0.107
2	4	0.215
3	6	0.299
4	8	0.402
5	10	0.507

Table 3: Interpretation of FTIR Spectrum

S.NO	Wave number in formulation (cm^{-1})		Characteristic Wave number range (cm^{-1})	Bond nature and bond attributed
	Pure drug	Optimized formulation		
1	3195	3057	3300-2500	O-H stretching Carboxylic acids
2	1643	1669	1760-1630	C=O stretching Carboxylic acids
3	1476	1463	1600-1400	C-C stretch in ring aromatics
4	1120	1126	1320-1000	C-O stretch Esters
5	990	957	900-675	C-H oop aromatics
6	814	832	1000-650	=C-H bend Alkenes

Table 4: Pre-compression parameters

Formulations	Bulk Density (gm/cm^2)	Tap Density (gm/cm^2)	Carr's Index (%)	Hausner's ratio	Angle of Repose(Θ)
F_1	0.45	0.55	18.18	1.22	27.91
F_2	0.47	0.55	14.54	1.17	28.23
F_3	0.50	0.58	13.79	1.16	29.34
F_4	0.46	0.55	16.36	1.19	26.71

F_5	0.50	0.58	13.79	1.16	29.34
F_6	0.47	0.55	14.54	1.17	28.23
F_7	0.50	0.58	13.79	1.16	29.34
F_8	0.41	0.50	18	1.21	26.78
F_9	0.41	0.50	18	1.21	26.78

Table 5: Post-Compression parameters

Formulation code	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Disintegration Time (sec)	Friability (%)	Assay (%)
F1	99	2.5	2.59	20.33	0.43	97.23
F2	104	2.6	2.64	22.66	0.34	98.55
F3	99	2.5	2.59	30.33	0.49	98.16
F4	101	2.6	2.58	19.00	0.47	99.34
F5	102	2.3	2.59	30.33	0.49	98.16
F6	103	2.7	2.64	22.66	0.34	98.55
F7	102	2.5	2.59	30.33	0.49	98.16
F8	100	2.6	2.56	17.00	0.34	99.25
F9	102	2.5	2.56	17.00	0.34	99.25

Table 6: *In-vitro* dissolution studies of all formulations

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
2	15.46	10.83	49.72	24.37	13.45	28.45	39.5	12.51	7.22
4	26.63	26.72	60.16	31.68	25.67	35.28	46.35	26.38	11.52
6	35.64	36.16	68.15	49.37	31.73	48.9	56.28	35.17	29.36
8	40.38	47.46	72.56	58.35	34.56	66.83	69.71	47.37	35.2
10	46.44	58.57	78.41	74.37	41.91	72.54	76.26	54.96	49.65
15	53.64	68.25	83.27	81.34	62.48	78.17	80.14	62.56	61.1
20	69.82	73.19	87.45	88.18	76.89	82.45	85.26	78.35	68.99
25	75.67	86.87	91.35	94.65	81.19	87.16	89.54	82.34	72.58
30	80.56	90.16	94.26	98.16	89.5	92.18	95.28	89.26	79.56

4. Conclusion

In the present work, an attempt has been made to develop fast disintegrating tablets of Dofetilide. In the present work Sodium starch glycollate, Cross povidone and Cross carmellose sodium were employed as super disintegrating agents to enhance the solubility and dissolution rate of selected drug molecule. All the formulations were prepared by direct compression method using 6mm punch on 8 station rotary tablet punching machine. The blend of all the formulations showed good flow properties such as angle of repose, bulk density, tapped density. The prepared tablets were shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations F4 formulation showed maximum % drug release i.e., 98.16 % in 30 min hence it is considered as optimized formulation. The F4 formulation contains Cross povidone as super disintegrate in the concentration of 5 mg.

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