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Formulation and *In-vitro* Evaluation of Daclatasvir Dihydrochloride Oral Dispersible Tablets

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A B S T R A C T

In the present work, an attempt has been made to develop fast disintegrating tablets of Daclatasvir dihydrochloride. In the present work Solutab, Polyplasdone XL and Explotab were employed as super disintegrating agents to enhance the solubility and dissolution rate of selected drug molecule. Camphor was employed as sublimating agent, due to presence of camphor maximum pores will be formed. As the numbers of pores were more the body fluid will penetrates more easily. All the formulations were prepared by direct compression method using 8mm punch on 8 station rotary tablet punching machine. The blend of all the formulations showed god 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 F8 formulation showed maximum % drug release i.e., 99.23% in 30 min hence it is considered as optimized formulation. The F8 formulation contains Explotab as super disintegrate in the concentration of 20 mg.

Keywords: Daclatasvir dihydrochloride, Sublimating agent, camphor, Solutab, Polyplasdone XL and Explotab.

A R T I C L E I N F O

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1. Introduction

ODTs are also called as or dispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets and rapid melts. However, of all the above terms, United States pharmacopoeia (USP) approved these dosage forms as ODTs. The European

Pharmacopoeia has used the term or dispersible tablet for tablets that disperses readily within 3 minutes in the mouth before swallowing. United States Food and Drug Administration defined ODT as "A solid dosage form containing a medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue." The disintegration time for ODTs generally ranges from several seconds to about a minute

2. Materials and Methods

Daclatasvirdihydrochloride, Microcrystalline cellulose, Explotab, Solutab, Polyplasdone HCl, Magnesium stearate, Talc chemicals were Laboratory grade made of SD Fine chemicals Pvt Ltd

Formulation of fast dissolving tablets of Daclatasvirdihydrochloride:

Optimization of camphor concentration:

Concentration of camphor should be optimized initially by keeping all the ingredients constant. Camphor was used in the concentration of 20, 40 and 60 mg.

Preparation of tablets:

Composition of Daclatasvirdihydrochloride fast dissolving Tablets by direct compression is shown in table 6 all the ingredients were weighed. Required quantity of drug and excipient 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 5mg Daclatasvir dihydrochloride and other pharmaceutical ingredients. Total weight of tablet was found to be 100mg.

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:

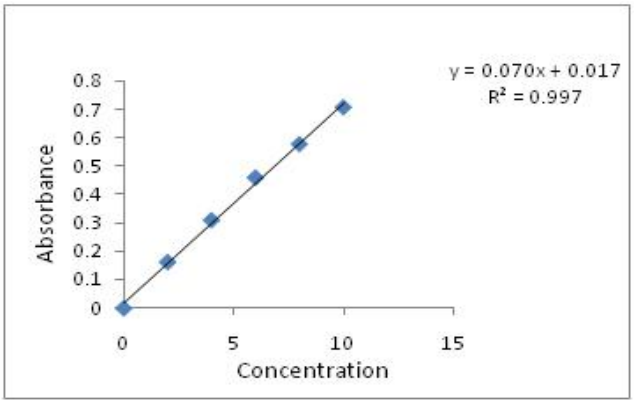

Figure 1: Standard graph of Daclatasvirdihydrochloride in pH 6.8 Phosphate buffer

It was found that the estimation of Daclatasvir dihydrochloride by UV spectrophotometric method at λ_{max}274 nm 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.

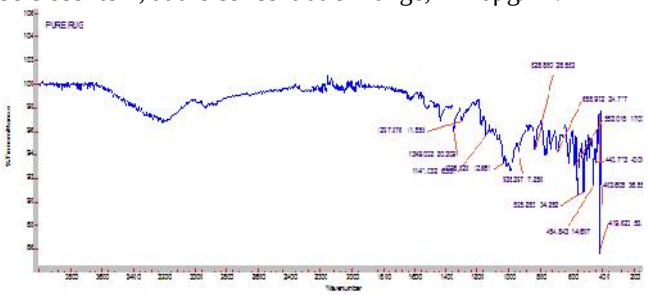

Figure 2: FT-TR Spectrum of Daclatasvir dihydrochloride pure drug.

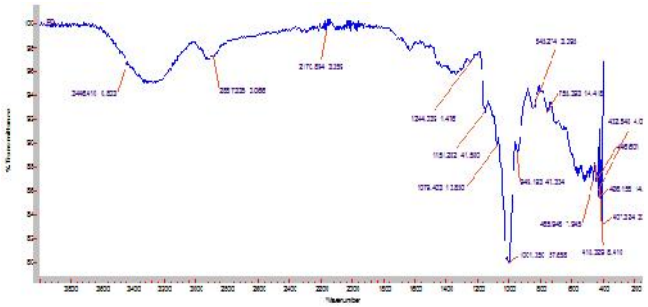

Figure 3: 3FT-TR Spectrum of Optimized formulation.

From the FTIR data it was evident that the drug and super disintegrates, other excipients doses not have any interactions**.** Hence, they were compatible.

Pre-compression parameters:

The data were shown in Table 5t. The values for angle of repose were found in the range of 26.68°- 29.34°. Bulk densities and tapped densities of various formulations were found to be in the range of 0.41 to 0.50 (gm/cc) and 0.50 to 0.58 (gm/cc) respectively. Carr's index of the prepared blends fall in the range of 13.79% to 18.18%.The Hausner ration fall in range of 1.16 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.

Optimization of concentration of camphor:

The concentration of camphor was optimized based on the number of pores formed. The tablets were prepared by keeping the concentration of the entire ingredients constant and changing the concentration of camphor. The concentration of camphor was fixed as 40 mg.

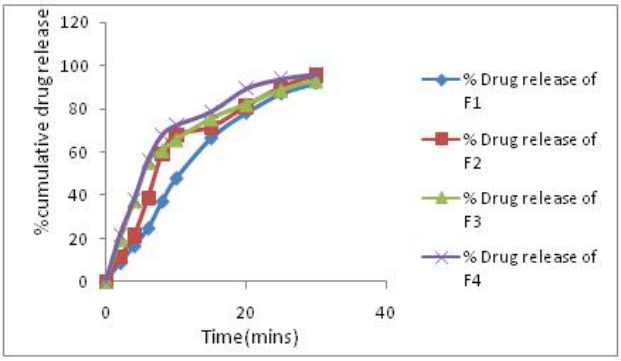

Figure 4: Dissolution profile of formulations prepared with Solutab as super disintegrate.

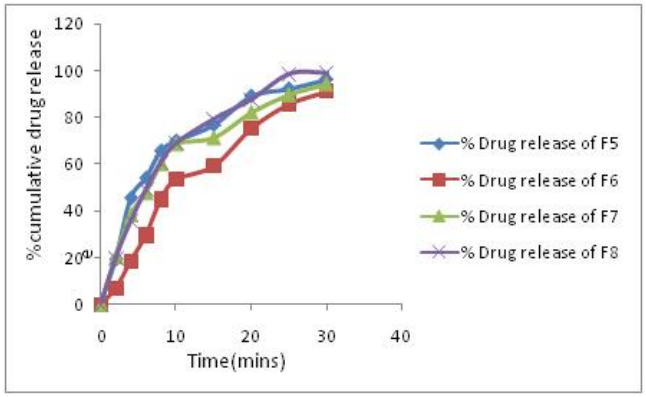

Figure 5: Dissolution profile of formulations prepared with Explotab as super disintegrate.

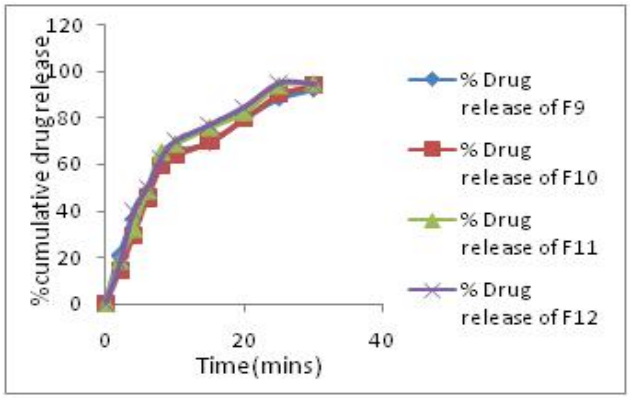

Figure 6: Dissolution profile of formulations prepared with Polyplasodne XL as super disintegrate.

Table 1: Optimization of camphor concentration

Ingredients	F1	F2	F3
Daclatasvirdihydrochloride	30	30	30
Explotab	15	15	15
Camphor	20	40	60
Mg. stearate	2	2	2
Talc	2	2	2
Mcc 102	56	36	16
Total weight	100	100	100

Table 2: Composition of various tablet formulations

Ingredient	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}
Daclatasvirdihydrochloride	30	30	30	30	30	30	30	30	30	30	30	30
Solutab	5	10	15	20	-	-	-	-	-	-	-	-
Explotab	-	-	-	-	5	10	15	20	-	-	-	-
Polyplasodne XL	-	-	-	-	-	-	-	-	5	10	15	20
Camphor	20	20	20	20	20	20	20	20	20	20	20	20
Talc	2	2	2	2	2	2	2	2	2	2	2	2
Mg. Stearate	2	2	2	2	2	2	2	2	2	2	2	2
MCC pH102	66	61	56	51	66	61	56	51	66	61	56	51
TOTAL	100	100	100	100	100	100	100	100	100	100	100	100

Table 3: Concentration and absorbance obtained for calibration curve of Daclatasvir dihydrochloride in pH 6.8 Phosphate buffer

S. No.	Concentration (µg/ml)	Absorbance* (at 274 nm)
1	2	0.163
2	4	0.311
3	6	0.461
4	8	0.579
5	10	0.709

Table 4: FTIR interpretation table

S.NO	Wave number in formulation (cm^{-1})		Characteristic Wave number range (cm^{-1})	Bond nature and bond attributed
	Pure drug	**Optimized formulation**		
1	2887	3446	3300-2500	O-H stretching Carboxylic acids
2	1297	1244	1320-1000	C-O Stretch Esters
3	938	949	900-675	C-H oop aromatics

4	828	845	1000-650	=C-H bend Alkenes

Table 5: Pre-compression parameters

Formulations	Bulk Density (gm/cm^2)	Tap Density (gm/cm^2)	Carr's Index (%)	Hausner 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
F10	0.42	0.51	18.24	1.20	26.68
F11	0.48	0.56	18.12	1.21	26.70
F12	0.41	0.54	18.11	1.22	26.71

Table 6: Post-Compression parameters

FD	Weight variation(mg)	Hardness (kg/cm^2)	Thickness (mm)	Disintegration Time (sec)	Friability (%)	Assay (%)
F_1	105	2.5	3.59	20.33	0.43	97.23
F_2	104	2.6	3.64	22.66	0.34	98.55
F_3	110	2.5	3.59	30.33	0.49	98.16
F_4	109	2.6	3.58	19.00	0.47	99.34
F_5	99.4	2.3	3.59	30.33	0.49	98.16
F_6	102	2.7	3.64	22.66	0.34	98.55
F_7	101	2.5	3.59	30.33	0.49	98.16
F_8	107	2.6	3.56	17.00	0.34	99.25
F_9	102	2.5	3.56	17.00	0.34	99.25
F10	103	2.4	3.55	15.99	0.43	98.6
F11	102.4	2.8	3.45	15.00	0.54	98.7
F12	98.5	2.5	3.54	16.76	0.43	98.5

Table 7: *In-vitro* dissolution data

Time(Min)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
2	8.65	11.24	19.52	21.53	19.45	6.78	20.62	19.81	20.89	14.21	18.27	16.28
4	16.45	21.34	37.47	37.89	45.66	18.54	38.35	35.7	36.43	29.19	32.18	39.47
6	24.64	38.79	55.48	56.38	54.16	29.73	47.8	49.25	48.18	45.32	48.67	49.58
8	37.11	58.99	60.93	68.06	65.78	45.04	60.24	60.92	59.89	59.13	65.18	62.35
10	47.87	67.88	65.85	72.52	70.01	53.56	68.73	69.08	65.53	63.63	68.77	69.78
15	66.59	71.46	75.54	78.88	76.88	59.25	71.34	79.44	69.43	69.71	75.79	76.82
20	78.34	81.23	82.33	89.56	89.26	75.41	82.17	87.9	79.98	79.27	82.35	84.54
25	87.22	89.98	88.89	94.09	92.35	85.85	89.75	98.83	88.52	89.86	93.79	94.76
30	92.21	95.78	93.23	96.34	96.39	91.23	94.32	99.23	92.38	93.56	94.68	94.21

Discussion

Literature review was carried out regarding chewable tablets, from that Daclatasvirdihydrochloride was selected as model drug and Polyplasodne XL, Explotaband Solutab were selected as polymers. Daclatasvir dihydrochloride, also known as L-deprenyl, is a substituted phenethylamine. At normal clinical doses, it is a selective irreversible MAO-B inhibitor. In larger doses, it loses its specificity and also inhibits MAO-A. It is available in pill form under many brand names and is used to reduce symptoms in early-stage Parkinson's disease. Analytical profile of drug molecule was established in 6.8 pH phosphate buffer and standard calibration curve was plotted by taking different concentrations. The drug and excipient comatability studies were carried out by using FTIR spectroscopy. From the studies it was evident that the drug and excipients are compatable with each other. Tablets were formulated with varying concentrations of Polyplasodne XL, Explotab and Solutab. The formulated oral dispersible tablets were evaluated for various physical parameters. The in-vitro dissolution study demonstrated that oral dispersible tablets of Daclatasvir dihydrochloride prepared with 20mg maize starch shown maximum drug release. Based on the results of evaluation tests formulation coded F8 was concluded as best formulation.

4. Conclusion

In the present work, an attempt has been made to develop fast disintegrating tablets of Daclatasvir dihydrochloride. In the present work sodium Solutab, Polyplasdone XL and explotab were employed as super disintegrating agents to enhance the solubility and dissolution rate of selected drug molecule. Camphor was employed as sublimating agent, due to presence of camphor maximum pores will be formed. As the numbers of pores were more the body fluid will penetrates more easily. All the formulations were prepared by direct compression method using 8mm punch on 8 station rotary tablet punching machine. The blend of all the formulations showed god 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 F8 formulation showed maximum % drug release i.e., 99.23 % in 30 min hence it is considered as optimized formulation. The F8 formulation contains Explotab as super disintegrate in the concentration of 20 mg.

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