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Research

Formulation And *In Vitro* Evaluation Of Mouth Dissolving Tablets Of Daclatasvirdi Hydrochloride

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Abstract

The mouth dissolving tablets has various advantages which has a triat of is a super distintegrant made from potato starch by carboxymethylation and crosslinking for tablets and other oral solid disintegrants called Explotab. The Daclatasvir Dihydrochloride mouth dissolving capsules have been organized the use of the fast compression technique. There had been a complete of evaluation used to consider the tablets, inclusive of the factor of rest, hardness, thickness, tapped density, carr's index, hausner's ratio, weight variation, hardness, friability and the drug release. The half-life of the third-generation (F3) Daclatasvir Dihydrochloride drug in vitro was once estimated to be happening 19 seconds. The drug release pattern had been released under 30minutes. Studies the using of Fourier transmission infrared spectroscopy (FTIR) indicates that there are possible interactions between the drug and any of the formulated ingredients. The maximum water absorption ratio was shown by formulation F3 showed 98%. Water absorption ratio is propo1tional to dissolution rate profile as higher the water absorption ratio Higher the dissolution.

Keywords: Solutab, Explotab, orally disintegrating tablets & Fourier radically change infrared spectroscopy studies.

INTRODUCTION

The oral route is the most popularly popular technique of affiliation due to its obvious ease of use, conservatism, and necessary societal significance. The most apparent disadvantage of the normally used oral estimates structures, such as drugs and holders, is situation in gulping, main to tolerant contradiction, specifically in pediatric and geriatric patients1. Patients who are ill and bedridden are now not the solely ones who can gain

from this; energetic sufferers who are working or visiting are additionally affected, specifically these who do not drinkwater.2 The improvement of higher orally disintegrating pills (ODTs) has attracted a lot of interest in latest years. Many people, particularly these who have bother gulping, admire pills that dissolve in the mouth as an alternative than in the stomach. This case of dysphagia is portrayed. Difficulty swallowing (or dysphagia) is frequent during all age groups, however is greater familiar in these who are younger, older, much less mobile, have negative coordination, intellectual fitness issues, or have issues with regurgitation or growth[1-5].The availability of harsh prescriptions throughout a number agencies is extended via ODTs with super flavor and taste.

The advantages of each dry and liquid counting are mixed in this technique of calculation. Ingenious ODT improvements take more than one medicines into account, have a exceptional flavor, and do not depart a terrible style or residue administration. Bioavailability problems with prescribed drugs that are hard to dissolve in water have caused lookup into whether or not or now not ODT can enhance the dissolution profile of prescription and medicine for hepatic processing.

Tablets that dissolve in the mouth are regarded through arrange of names, which includes or odispersible, speedy separating, mouth dissolving, rapid disintegrating, quickly dissolving, permeable, and rapimelts. Despite this, the unique phrases above areal viewed ODTs by means of the US pharmacopoeia (USP)[6.7.] Recently, the US Food and Prescription Association (FDA) defined ODT as "As table estimations shape containing useful tongue." Breakdown recollections vary from a few seconds to a couple of minutes for most ODTs.

MATERIALS AND METHODS

The materials used in this current research work are procured from reliable sources of Daclatasvir dihydrochloride, Bristol Myers Squibb, Polyplasdone XL, solutab, explotab, aspartame, talc, magnesium stearate and MCC are obtained from Oxford Laboratories Pvt Ltd., Mumbai, INDIA. All other reagents and chemicals used in this research work has been purchased from the reliable sources.

Construction of standard graph

100 mg of Daclatasvir Dihydrochloride was dissolved in 100 mL of pH 6.8 phosphate buffer to give a concentration in 1 mg/mL (1000 Lg/mL) 1 ml was taken and diluted to 100 ml with pH6.8 phosphate buffer to give a concentration of 0.01 mg/ml (10 Lg/ml). From this stock solution aliquots of 0.5 ml, 1 mL 1.5 ml, 2 ml, 2.5 ml, were pipette out in 10 ml volumetric flask and volume was made up to the mark with pH 6.8 phosphate buffer to produce concentration of 5, 10, 15, 20 and 25µg/ml respectively. The absorbance of each concentration was measured at respective Amax is 294.

Formulation development

Drug and different concentrations of super disintegrants (Polyplasdone XL, Solutab, Explo tab) and required ingredients were accurately weighed and passed through a40-meshscreentoget uniform size pa1ticles and mixed in a glass motor for 15 min[8-15].

Table 1: Formulation table showing various compositions

Ingredients	Formulations								
	Fl	**F2**	**F3**	**F4**	**FS**	**F6**	**F7**	**F8**	**F9**
Daclatasvir Dihydrochloride	60	60	60	60	60	60	60	60	60
PolyplasdoneXL	15	30	45	-	-	-	-	-	-
Solutab	-	-	-	15	30	45	-	-	-
Explotab	-	-	-	-	-	-	15	30	45
Aspaitame	10	10	10	10	10	10	10	10	10
Talc	5	5	5	5	5	5	5	5	5
Mgstreate	4	4	4	4	4	4	4	4	4
MCC	56	41	26	56	41	26	56	41	26
Total Weight	150	150	150	150	150	150	150	150	150

Thickness

The thickness of the tablets wasdete1mined by using Digital micrometer. 10 individual tablets from each batch were used and the results averaged.

Weight variation

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation 3 batches were calculated. It passes the test for weight variation test if not more than 2 of the individual tabletweightsdeviatefromtheaverageweightbymorethantheallowedpercentage deviation and none

deviate by more than twice the % shown. It was calculated on an electronic weighing balance.

Friability

The friability values of the tablets were dete1mined using a Roche-friabilator. Accurately weighed six tablets were placed in The Roche friabilator and rotated at 25 RPM for 4 min. Percentage friability was calculated using the following equation. Friability = ([wo-w]/wo)x 100

Drug content

The content of drug carried out by 5 randomly selected tablet so feach formulation. The 5 tablets were grinded to get powder, this powder was dissolve dinpH6.8 phosphate buffer by sonication for 30min and filtered through filter paper. The dmg content was analyzed spectrophotometricaly at 294nm using UV spectro photometer. Each measurement was carried out in triplicate and the average drug content was calculated.

Disintegration test

Six tablets were taken randomly from each batch and placed in USP disintegration apparatus baskets[17-23]. Apparatus was mn for 10 min. and the basket was lift from the fluid, obse1ve whether all of the tablets have disintegrated. Apiece of tissue paper folded

Wetting Time

Piece of tissue paper folded twice was placed in a small petridish containing 6ml of water. A water-soluble dye phenolphthalein was added to the petridish. The dye solution was used to identify the complete wetting of the tablet surface. A tablet was carefully placed on the surface of tissue paper in the petridish at room temperature[16].

Water Absorption Ratio(R)

The weight of the tablet before keeping in the petridish was noted (Wb) using digital balance. The wetted tablet from the petridish was taken and reweighed (Wa-) using the same [24-27]. The Water absorption ratio, R, was dete1mined according to the following equation: R = (Wa- Wb) / Wb*100)

RESULTS AND DISCUSSION

Calibration Curve of Daclatasvir Dihydrochloride

The regression coefficient was found to be 0.999 which indicates linearity with an equation of Y=0.023X-0.004. Hence Beer-Lambert's law was obeyed.

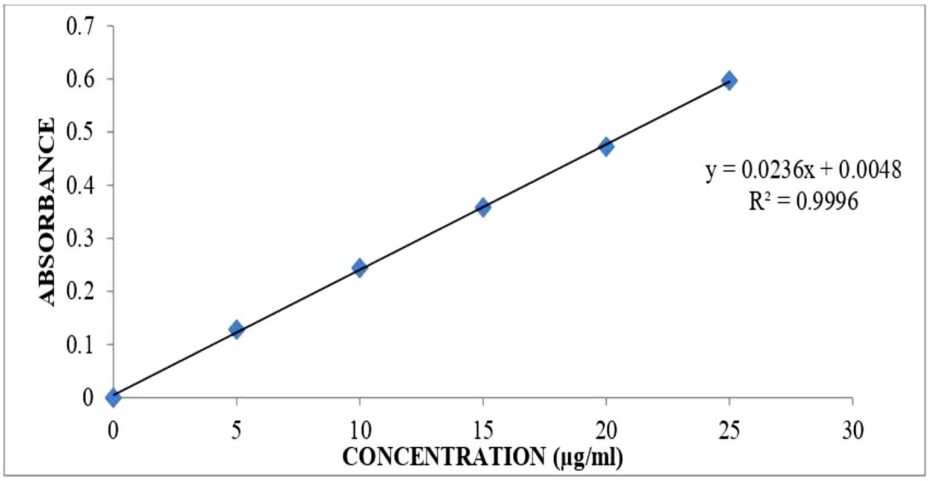

Fig 1: Standard curve of Daclatasvir Dihydrochloride

Method

In vitro dispersion time was determined by placing one tablet in a beaker containing 10 ml of pH 6.8 phosphate buffer at 37±0.5°c and the time required for complete dispersion was dete1mined.To check for reproducibility, the measurements were carried out in triplicates (n=3). The dispersion time was recorded using a stopwatch.

Dissolution test of Daclatasvir Dihydrochloride

Drug release from Daclatasvir Dihydrochloride tablets was determined by using dissolution test USP 24 type II (paddle). The parameters used for per fo1ming the dissolution were pH6.8 medium as the dissolution medium of quantity 900 ml.

Drug-Excipients compatibility studies

Dmg excipients compatibility studies were carried out by mixing the drug with various excipients in different propo1tions (in 1;1 ratio were to have maximum likelihood interaction between them) was placed in a vial, and closed with rubber stopper and sealed properly. Fourier Transfo1m Infrared Spectroscopy (FTIR) studies were perfumed on drug, optimized formulation using FTIR. The samples were ai1alyzed between wave numbers 4000 $cm^{-1}$and 550cm^{-1}.

Evaluation Of Pre-Compression Parameters of Powder Blend

Table 1: Evaluation of pre-compression parameters of powder blend

Formulation Code	Angleof Repose	Bulk Density (gm/mL)	Tapped Density (gm/mL)	Carr's Index(%)	Hausner's Ratio
Fl	27.06±0.02	0.58±0.06	0.66±0.07	12.12±1.13	1.11
F2	27.06±0.02	0.57±0.09	0.66±0.08	13.63±1.01	1.10
F3	26.57±0.02	0.56±0.05	0.65±0.04	13.84±0.35	1.08
F4	24.62±0.03	0.58±0.05	0.66±0.07	12.12±1.27	1.07
FS	24.42±0.01	0.58±0.05	0.69±0.02	13.04±1.05	1.10
F6	24.42±0.01	0.61±0.04	0.69±0.06	11.59±1.11	1,10
F7	24.51±0.02	0.62±0.04	0.67±0.04	7.46±1.36	1.07
F8	24.49±0.01	0.58±0.02	0.66±0.08	12.12±1.55	1.17
F9	24.45±0.03	0.58±0.04	0.66±0.02	12.12±0.35	1.08

For each formulation blend of drug and excipients were prepared and evaluated for various recompression parameters described earlier in methodology chapter. The bulk density of all formulations was found in the range of 0.56±0.05- 0.62±0.04 and tapped density was in the range of 0.65±0.04 - 0.69±0.06. The Carr's index and Hausner's ratio was calculated from tapped density and bulk density.

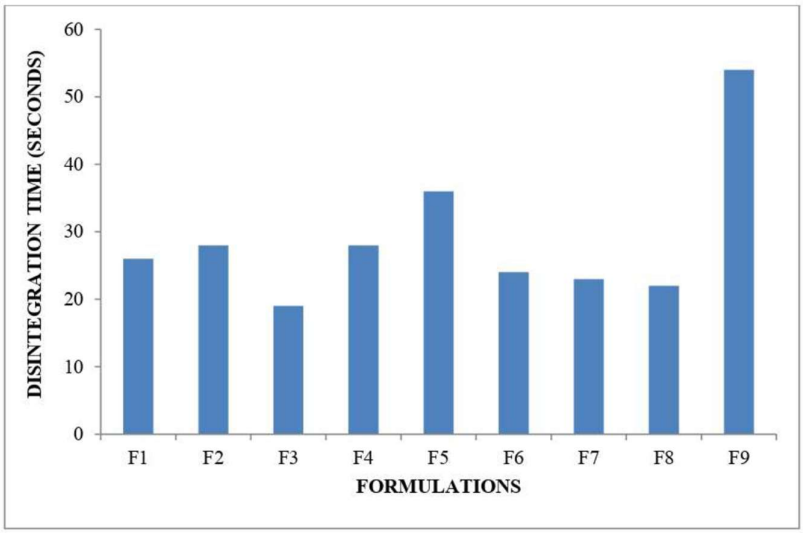

Fig 2 : *In vitro* Disintegration time

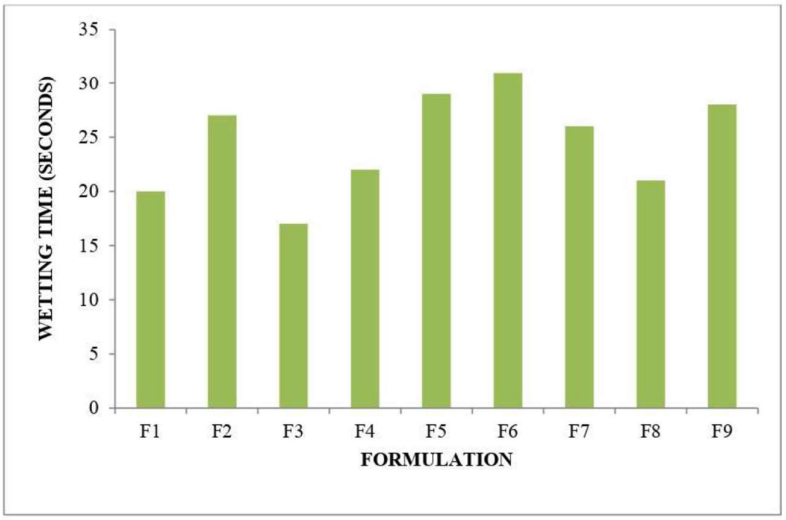

Fig 3: Wetting time

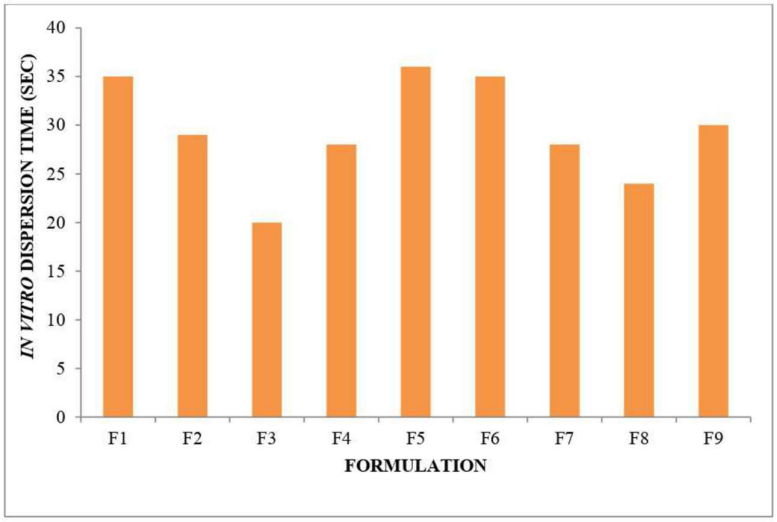

Fig 4: *In vitro* Dispersion Time

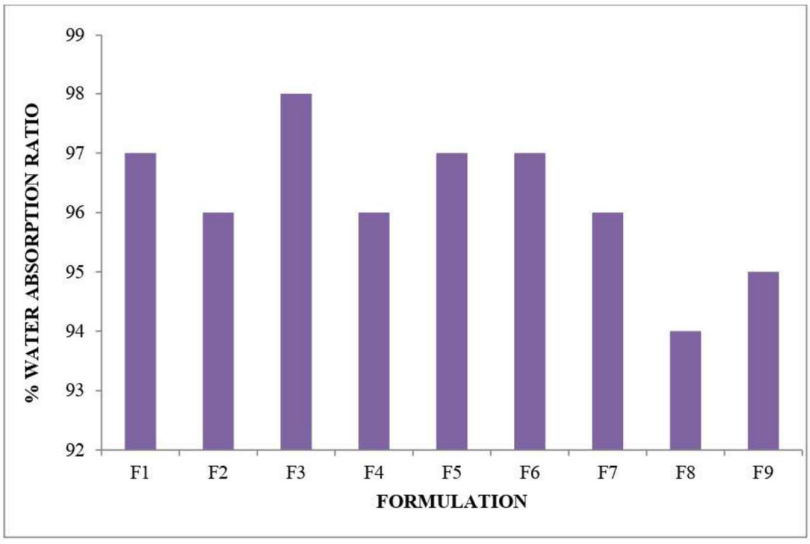

Fig 5: Water absorption ratio

In vitro disintegration studies showed from 19 to 54secs. These results indicate that the F3 fo1mulation which shown less disintegration time than remaining formulations. Wetting time to the time required to wet completely when kept motionless on the tissue paper in a petridish. All the FDT formulations were evaluated for their wetting time as per the procedure described in the method ology section, and the results are shown in table. The average wetting time for all the formulations was in the range of (17to31) seconds.

In vitro dispersion time

Daclatasvir Dihydrochloride Mouth Dissolving Tablets F3 formulation dispersed time was 20 secs. It was known that less dispersion time than other formulation. The In vitro dispersion time for all formulation was found to be in a range of 20 to36 seconds. All the fo1mulations were evaluated for water absorption ratio according to the procedure desc1ibed in methodology section and the results are shown in table. The maximum water absorption ratio was shown by formulation F3 showed 98%. Water absorption ratio is propo1tional to dissolution rate profile as higher the water absorption ratio Higher the dissolution as shown in the fig 2,3,4 & 5.

In vitro Dissolution profiles

The F3 formulation shows 99.42% dmg releasein 30min while using 45mg concentration of PolyplasdoneXL and disintegration time is 19 sec. In which increase of concentration of PolyplasdoneXL improved dissolution and decreased disintegration so it was optimized formulation. PolyplasdoneXL, Solutab and Explotab are three used as super disinter grants. Finally Concluded thatF3 formulation was the optimized Formulation as mentioned in the figure 6 & 7.

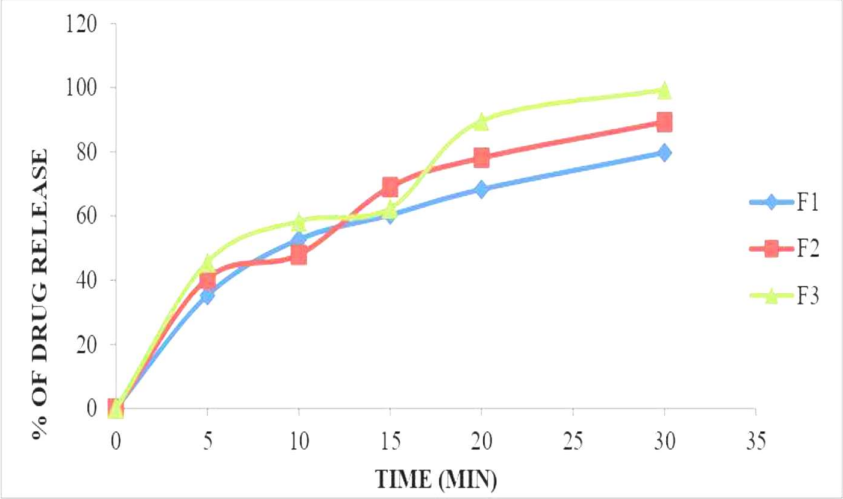

Fig 6: Dissolution profile of formulations Fl,F2,F3

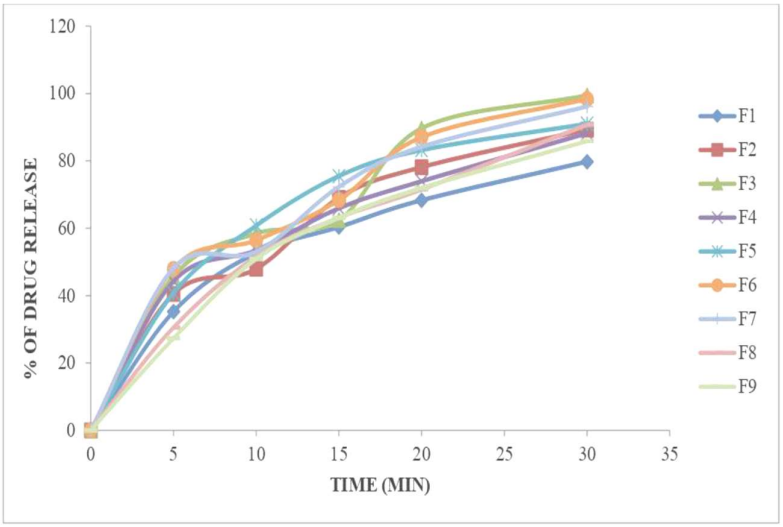

Fig 7: Dissolution profile of all formulations F1-F9

FTIR Results

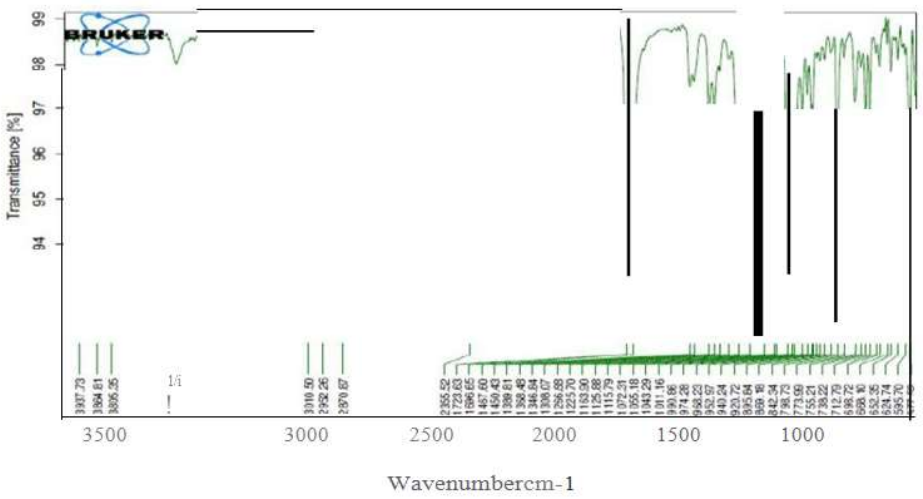

Fig 8: FTIR of Daclatasvir Dihydrochloride Pure Drug

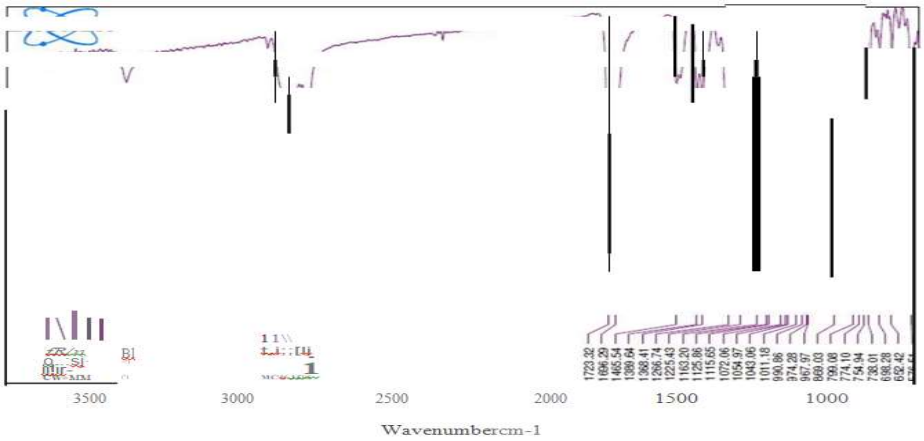

Fig 9: FTIR of Daclatasvir Dihydrochloride optimized formulation

Daclatasvir Dihydrochloride was mixed with propo1tions of excipients showed no color change providing no drug-excipient interactions as represented in the fig 8 & 9.

CONCLUSION

Conversely in the present investigation, all formulations of the pre and post compression parameters were found to be within limits. The formulation tablets showed compliance for various physicochemical parameters viz. hardness, friability, weight variation, content uniformity and disintegration time. The dmg content was within acceptable range which ensured dose unif01mity in the fo1mulation.Preformulationstudies of Daclatasvir Dihydrochlolide were pe1fo1med; the FT-IR analysis revealed that the super disintegrants and excipients used were compatible with Daclatasvir Dihydrochloride. Mouth dissolving tablets of Daclatasvir Dihydrochloride is to be prepared by direct compression technique using super disintegrants namely PolyplasdoneXL, Solutab and Explotab. Among stall the formulations, formulation containing PolyplasdoneXL as super disintgrants is for filling all the parameters satisfactorily. It has shown excellent *in vitro* disintegration compared to other super disintegrants. Apart from all thefo1mulations, F3 fo1mulation showed maximum drug release (99.42%) at the end of 30min.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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