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FORMULATION, *IN VITRO* DRUG RELEASE AND STABILITY STUDIES OF CLOPIDOGREL RAPIDLY DISINTEGRATING TABLETS

R. Krishna Kumari*[1], P. Bharathi[1], CH. Saritha Reddy[1]

[*1]Department of Pharmacy, B. A and K. R College of Pharmacy, Ongole, Andhra Pradesh, India.

ABSTRACT

The aim of study to develop a pharmaceutically stable, cost effective and quality improved formulation of Clopidogrel tablets. Rapidly disintegrating tablets of Clopidogrel can be prepared by Mass Extrusion technique using the different superdisintegrants, namely Sodium starch glycolate, Avicel PH 102, and Low Hydroxy Propyl Cellulose. The tablets were evaluated for Shape and Color of tablets, Uniformity of thickness, Hardness test, Weight variation test percentage friability, Drug content uniformity, Wetting time, Water absorption ratio, *In vitro* dispersion time, Disintegration time, *In vitro* dissolution studies and Stability studies. Amongst all the formulations, formulation containing sodium starch glycolate as superdisintegrants is fulfilling all the parameters satisfactorily. The formulations F3, F6, F9 were selected for stability studies on the basis of their better and satisfactory evaluation studies parameter. These formulations showed not much variation in any parameter even after the period of 30 days. From these results it was concluded that, formulations F3, F6, F9 are found to be stable and retained their original properties.

KEYWORDS

Rapidly disintegrating tablets, Clopidogrel, Different superdisintegrants and Mass Extrusion technique.

Author of correspondence:
R. Krishna Kumari,
Department of Pharmacy,
B.A and K.R College of Pharmacy,
Ongole, Andhra Pradesh, India.

Email: krishnar.kumari3@gmail.com.

INTRODUCTION

Oral drug delivery is the most desirable and preferred method of administering therapeutic agents for their systemic effects. For many drug substances, conventional immediate release formulations provide clinically effective therapy while maintaining the required balance of pharmacokinetic and pharmacodynamic profiles with an acceptable level of safety to the patient. Consumer satisfaction is the buzzword of the current millennium, and moment to achieve it has already begun in the pharmaceutical

industry. An inability or unwillingness to swallow solid oral dosage forms such as tablets and poor taste of medicine are some of the important reasons for consumer dissatisfaction[1].

Recent developments in technology have presented viable alternatives for the patients who may have difficulty in swallowing tablets or liquids. Traditional tablets and capsules administered with an 8-oz. glass of water may be inconvenient or impractical for some patients. For example a very elderly patient may not be able to swallow a daily dose of tablets. An eight year old child with allergies could use a more convenient dosage form of antihistamine syrup. A schizophrenic patient in the institution setting can hide a conventional tablet under his or her tongue to avoid his/ her daily dose of atypical antipsychotic. A middle-aged women undergoing radiation therapy for breast cancer may be too nauseous to swallow her h_2-blocker[2].

To overcome these drawbacks, Fast Dissolving Tablets (FDT) or orally disintegrating tablets (ODT) has emerged as alternative oral dosage forms. These are novel types of tablets that disintegrate/dissolve/ disperse in saliva within few seconds. According to European Pharmacopoeia, the orally dispersible tablet should disperse/disintegrate in less than three minutes. The basic approach used in development of FDT is the use of super disintegrants like Crospovidone (Polyplasdone XL-10), Sodium starch glycolate (Primo gel, Explotab) and Pregelatinized starch (Starch-1500) etc. which provide instantaneous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva.

The bioavailability of some drugs may be increased due to absorption of drugs in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach. Moreover, the amount of drug that is subjected to first pass metabolism is reduced as compared to standard tablets[3]. Over the past three decades, FDT have gained much attention as a preferred alternative to conventional oral dosage forms such as tablets and capsules. FDT is a solid dosage form that disintegrates and dissolves in the mouth (either on or beneath the tongue or in the buccal cavity) without water within 60 seconds or less[4].

MATERIALS AND METHOD

Materials

Clopidogrel was obtained from Orchid chemical labs, Chennai, India. Eudragit E 100, Sodium Starch Glycollate, Microcrystalline cellulose and Lactose were purchased from Karnataka Fine Chem, Bangalore, India. Magnesium Stearate and Talc was purchased from SD Fine Chem. Ltd, Mumbai, India. Starch was purchased from Finar chemicals, Ahmadabad, India. All other chemicals and ingredients were used for study are of Analytical grade.

Method

Preparation of Clopidogrel rapidly disintegrating tablets[5]

The drug is mixed with powdered Eudragit E-100 in a suitable ratio. Then 10% ethanol is added to the above mixture in a glass beaker. The consistency of the above solution is reduced to get gel type of preparation, and then it is extruded through a syringe on clean glass slab. After extrusion of the gel, dried overnight till ethanol is evaporated and solidified material (gel) crushed into granules using a mortar. The granules are passed through a sieve and collected, blend with excipients. Then blend is subjected for tablet formulation (Table No.1).

EVALUATION PARAMETERS

Pre-formulation Studies

Compatibility studies of Clopidogrel and formulation components

The compatibility of drug and polymers under experimental conditions is important prerequisite before formulation. It is therefore necessary to confirm that the drug does not react with the polymer and excipients under experimental conditions and affect the shelf life of product or any other unwanted effects on the formulation. Infrared spectrum of the representative Clopidogrel and excipients were taken. The study was conducted on Thermo Nicolet (FTIR-200). The spectra's were run from 4000 nm to 500 nm wave number.

Precompression Parameters

Angle of Repose (θ)

The frictional forces in a loose powder or granules can be measured by the angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane[6, 7].

$$\tan \theta = h/r$$

$$\theta = \tan^{-1} (h/r)$$

Where,

θ is the angle of repose

h is the height

r is the radius.

The granules were allowed to flow through the funnel fixed to a stand at definite height. The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

Bulk Density

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. The accurately weighed amount of sample taken in a 25ml measuring cylinder of Borosil measured/recorded the volume of packing and tapped 100 times on a plane hard wooden surface and tapped volume of packing recorded and LBD and TBD calculated by following formula:

LBD (Loose Bulk Density) = Mass of Powder/ Volume of Packing

TBD (Tapped Bulk Density) = Mass of Powder/ Tapped Volume of Packing

Percentage Compressibility

Percent compressibility of powder mix was determined by Carr's compressibility index calculated by following formula.

Carr's index (%) = [(TBD - LBD) x 100] / TBD

Post Compression Parameters

Shape and colour of tablets

Uncoated tablets were examined under a lens for the shape of the tablet and color was observed by keeping the tablets in light[8].

Uniformity of thickness

Three tablets were picked from each formulation randomly and thickness was measured individually. It is expressed in mm and standard deviation was also calculated. The tablet thickness was measured using dial-caliper (Mitutoyo, Japan)[9].

Hardness test

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm^2. Three tablets were randomly picked and hardness of the same tablets from each formulation was determined. The mean and standard deviation values were also calculated[9].

Friability Test[10]

The friability of tablets was determined using Roche Friabilator. It is expressed in percentage (%). Ten tablets were initially weighed ($W_{initial}$) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (W_{final}). The % friability was then calculated by,

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100$$

% Friability of tablets less than 1% are considered acceptable.

Drug Content Uniformity

One tablet was weighed and powdered. The whole amount of powdered tablet was transferred into a 100 ml volumetric flask. Add 0.1N Hcl up to the mark. After few minutes the solution was filtered; rejecting first few ml of the filtrate. 2ml of filtrate was taken in a 25 ml volumetric flask and diluted up to the mark with 0.1N Hcl and analyzed spectrophotometrically at 305 nm. The concentration of Clopidogrel (in μg/ml) was calculated by using the standard calibration curve of Clopidogrel Drug content in mg was calculated by using formula;

$$\frac{\text{Concentration in } \mu g/ml \times 100 \times 25}{2 \times 1000}$$

Drug content claim was 10mg per tablet. This procedure was followed for 5 tablets from each formulation. The mean and standard deviation values were also calculated.

Weight Variation Test

Ten tablets were selected randomly from each formulation and weighed individually to check for weight variation. The US Pharmacopoeia allows a little variation in the weight of a tablet. In all the

formulations the tablet weight is less than 324 mg; hence 7.5% weight variation is allowed[9].

Water Absorption Ratio

A piece of tissue paper folded twice was placed in a small Petridish containing 6ml of distilled water. A tablet was put on the paper and time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R, was determined using equation –

$$R = 100 \times Wa - Wb/Wb$$

Where,

Wb = weight of the tablet before water absorption

Wa = weight of the tablet after water absorption

Three tablets from each formulation were performed and standard deviation was also determined[10].

Wetting time

The method was applied to measure tablet-wetting time. A piece of tissue paper folded twice was placed in a small Petridish (i.d. = 6.5 cm) containing 6 ml of water, a tablet was put on the paper, and the time for complete wetting was measured. Three trials for each batch were performed and standard deviation was also determined[11].

***In vitro* Dispersion Time**

In vitro dispersion time was measured by dropping a tablet in a measuring cylinder containing 6 ml of pH 6.8 (simulated saliva fluid). Three tablets from each formulation were randomly selected and *in vitro* dispersion time was performed. Standard deviation was also determined and *in vitro* dispersion time is expressed in seconds[11].

***In vitro* Disintegration Test**

The process of breakdown of a tablet into smaller particles is called as disintegration. The *in vitro* disintegration time of a tablet was determined using disintegration test apparatus as per I.P. specifications.

Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using pH 6.8 (simulated saliva fluid) maintained at $37^0 \pm 2^0$C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the pH 6.8 maintained at $37^0 \pm 2^0$C. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded[10].

In vitro Dissolution Studies

In vitro release studies were carried out using USP-type II dissolution apparatus (paddle type). Two objectives in the development of *in vitro* dissolution tests are to show (1) that the release of the drug from the tablet is as close as possible to 100% and (2) that the rate of drug release is uniform batch to batch and is the same as the release rate from those batches proven to be bioavailable and clinically effective[12].

Stability Studies

Stability of a drug has been defined as the ability of a particular formulation, in a specific container, to remain within its physical, chemical, therapeutic and toxicological specifications. The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, and enables recommended storage conditions, re-test periods and shelf lives to be established. In the present study, stability studies were carried out at 25^0C/60% and 40^0C /75% RH for a specific time period up to 30 days for selected formulations[13].

RESULTS AND DISCUSSION

Preformulation Studies

Drug-excipients Compatibility Studies

To study the compatibility of the drug with various superdisintegrants, IR spectra of drug and formulation components were carried out. The IR spectra of the drug and all excipients were shown in Figure No.1 to 5. The characteristics absorption peaks of Clopidogrel were obtained at 3391.48, 2634.50, 1597.18, and 676.19. The peaks obtained in the spectras of each excipient correlate the peaks of drug spectrum. By correlation, it indicates that drug (Clopidogrel) is compatible with the components.

Formulation Design

Rapidly disintegrating tablets of Clopidogrel were prepared to enhance overall bioavailability by using mass extrusion method. Total nine formulations were prepared in which the concentrations of the superdisintegrants is varied to evaluate the effect on

the disintegration time of Clopidogrel mouth dissolving tablets. The composition of nine formulations is given in Table No.1.

EVALUATION OF TABLETS

Pre-compression Parameters

Angle of Repose (θ)

Table No.2 shows the results obtained for angle of repose of all the formulations. The values were found to be in the range of 25^0.22' to 30^0.17'. All formulations showed the angle of repose within 30^0.

Bulk Density

Both loose bulk density and tapped bulk density results are shown in Table No.2. The loose bulk density and tapped bulk density for all the formulations varied from 0.56 gm/cm^3 to 0.62gm/cm^3 and 0.67 gm/cm^3 to 0.73gm/cm^3 respectively. The values obtained lies within the acceptable range and not large differences found between loose bulk density and tapped bulk density. This result helps in calculating the % compressibility of the powder.

Percentage Compressibility

This percent compressibility of powder mix was determined by Carr's compressibility index. Table No.2 shows result obtained for percentage compressibility. The percent compressibility for all the nine formulations lies within the range of 13.432 to 17.808. All formulations are showing good compressibility.

Post-compression Parameters

Shape and Color of Tablets

Randomly picked tablets from each formulation batch examined under lens for shape and in presence of light for color. Tablets showed flat, circular shape in white color.

Thickness Test

The thickness of the tablets was measured by using dial caliper by picking the tablets randomly. The mean values are shown in Table No.3. The values are almost uniform in all formulations. Thickness was found in the range from 2.90 mm to 3.18 mm respectively.

Hardness Test

The results of hardness are given in Table No.3. Hardness test was performed by Monsanto tester. Hardness was maintained to be within 2.90 kg/cm^2 to 3.87 kg/cm^2, as these tablets are rapidly disintegrating. The lower standard deviation values indicated that the hardness of all the formulations were almost uniform and possess good mechanical strength with sufficient hardness.

Friability Test

The study results are tabulated in Table No.3 was found well within the approved range (<1%) in all the formulation. Results revealed that the tablets possess good mechanical strength.

Weight Variation Test

The percentage weight variation for all the formulation is tabulated in Table No.3. All the tablets passed weight variation test as the % weight variation was within the pharmacopoeial limits of ±7.5%. It was found to be from 298.6 to 301.0 mg. The weight of all the tablets was found to be uniform.

Drug Content Uniformity

The content uniformity was performed for all the nine formulations and results are shown in Table No.3. Five trials from each formulation were analyzed spectrophotometrically. The mean value and standard deviation of all the formulations were calculated. The drug content of the tablets were found between 9.700±0.148 mg to 9.925±0.067 mg of Clopidogrel. The results indicated that in all the formulations the drug content was uniform. The cumulative percentage drug released by each tablet in the *in vitro* release studies were based on the mean content of the drug present in the respective tablet.

Wetting Time

Wetting is closely related to inner structure of tablets. The record of the wetting time was shown in Table No.4. The wetting time in all the formulation was very fast. This may be due to ability of swelling and also capacity of absorption of water. L-HPC is having high water absorption capacity and cause swelling. L-HPC and starch glycolate absorbs water rapidly in the formulations and shows fast wetting time. This parameter also duplicates disintegration time in oral cavity as tablet is kept motionless on

tongue; hence correlation between wetting time and disintegration time in oral cavity can also be made.

Water Absorption Ratio

The water absorption ratio results are tabulated in Table No.4. The ratio values of formulations found in the range of 18.45 to 37.89. In this, as L-HPC quantity decreases, the water absorption also decreases due to less swelling property.

***In vitro* Disintegration Time**

The internal structure of tablets that is pore size distribution, water penetration into tablets and swelling of disintegration substance are suggested to be the mechanism of disintegration. The results are shown in Table No.5. This was determined as per I.P. for all the formulations. All formulations showed disintegration time less than 30 seconds.

***In vitro* Dispersion Time**

The values obtained are recorded in Table No.5. *In vitro* dispersion time is measured by the time taken to undergo uniform dispersion. Rapid dispersion within seconds observed in all the formulations. This indicates the L-HPC, Avicel PH 102 and Sodium starch glycolate showed best disintegrants in the prepared tablets. This *in vitro* dispersion time gives direct information regarding super-disintegrating nature of disintegrants used.

***In vitro* Dissolution Studies**

All the nine formulations were subjected for the *in vitro* dissolution studies using USP-type II dissolution apparatus (paddle type). The samples were withdrawn at different time intervals and analyzed at 234 nm. Cumulative drug release and cumulative % drug retained were calculated on the basis of mean amount of Clopidogrel present in the respective tablet. The results obtained in the *in vitro* drug release for the formulations F1 to F9 are tabulated in Table No.6. The plots are shown from Figure No.6 (a, b and c) for % cumulative drug release vs time.

Formulation F1, F2, F3, releases 89.83%, 91.10%, 96.20%, respectively, at end of 15 minutes. The rapid drug dissolution was observed in F4, F5, and F6, which release 85.11%, 88.71% and 90.44% respectively at end of 15 minutes. Formulation F7, F8, F9, releases 78.26%, 82.26% and 85.31%, respectively, at end of 15 minutes. This rapid dissolution might be due to fast breakdown of particles and rapid absorption of drug. The drug release was completely achieved in a shorter duration of time. In all the formulations the drug release was near to 100% within 15 minutes. High dissolution may also occur due to faster breakdown. F4, F5, F6, F7, F8 and F9 showed release variation probably due to slow breakdown of particles.

Stability Studies

The formulations F3, F6, F9 were selected for stability studies on the basis of their high cumulative % drug release and also results of *in vitro* disintegration time, wetting time, and *in vitro* dispersion studies. The stability studies were carried out at 25^0C/60% RH and 40^0C/75% RH for all the selected formulations up to 30 days. For every 10 days time interval the tablets were analyzed for drug content uniformity, hardness, *in vitro* disintegration time, friability and wetting time up to 30 days. These formulations showed not much variation in any parameter. The results obtained are tabulated in Table No.7 and Table No.8. From these results it was concluded that, formulations F3, F6, F9 are stable and retained their original properties.

Table No.1: Composition of rapidly disintegrating tablets of Clopidogrel

S.No	Ingredients (mgs)	Formulation code								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Clopidogrel	300	300	300	300	300	300	300	300	300
2	Sodium starch glycolate	15	22.5	30	--	--	--	--	--	--
3	Avicel PH 102	--	--	--	15	22.5	30	--	--	--
4	Low HPC	--	--	--	--	--	--	15	22.5	30
5	Eudragit E100	10	10	10	10	10	10	10	10	10
6	Lactose	259	251.5	244	259	251.5	244	259	251.5	244
7	Magnesium Stearate	3	3	3	3	3	3	3	3	3
8	Talc	3	3	3	3	3	3	3	3	3

Table No.2: Angle of repose, Loose bulk density, Tapped bulk density, Carr's compressibility index

S.No	Formulation code	Angle of Repose (θ)	Loose Bulk Density (gm/cm^3)	Tapped Bulk Density (gm/cm^3)	% Compressibility
1	F1	28.23	0.58	0.71	15.492
2	F2	27.31	0.57	0.70	14.285
3	F3	25.22	0.56	0.67	13.432
4	F4	29.37	0.61	0.72	16.666
5	F5	28.22	0.60	0.70	15.289
6	F6	27.37	0.59	0.69	14.285
7	F7	30.17	0.62	0.73	17.808
8	F8	29.19	0.61	0.71	15.492
9	F9	28.88	0.60	0.70	14.676

Table No.3: Evaluation of tablet parameters

S.No	Formulation Code	Thickness (n=3) (mm)	Hardness (n=3) (kg/cm^2)	Friability (%) (n=10)	Uniformity of Weight (n=10) (mg)	Drug Content (n=3) (mg)
1	F1	4.13±0.05	3.87±0.29	0.3633	501.0±2.013	9.790±0.148
2	F2	4.17±0.06	3.76±0.29	0.2103	500.5±2.153	9.825±0.113
3	F3	4.18±0.05	3.70±0.29	0.1356	500.5±2.652	9.925±0.067
4	F4	4.97±0.03	3.76±0.29	0.3496	598.6±2.88	9.889±0.176
5	F5	4.13±0.05	3.24±0.29	0.3035	500.0±1.032	9.900±0.031
6	F6	4.15±0.13	3.66±0.29	0.2103	500.1±1.272	9.918±0.021
7	F7	4.90±0.05	3.24±0.29	0.4739	500.1±2.171	9.700±0.148
8	F8	4.97±0.03	2.96±0.29	0.4200	499.4±3.045	9.835±0.113
9	F9	4.98±0.03	2.90±0.29	0.4187	499.6±2.197	9.876±0.054

Table No.4: Wetting time, water absorption ratio

S.No	Formulation Code	Wetting Time (n=3)	Water absorption ratio (n=3)
		Mean ± SD	***Mean ± SD***
1	F1	22.00 ± 1.12	27.81 ± 1.123
2	F2	18.00 ± 0.67	19.84 ± 0.663
3	F3	17.33 ± 1.55	18.45 ± 2.135
4	F4	24.67 ± 0.36	30.89 ± 1.637
5	F5	23.67 ± 0.55	29.89 ± 1.653
6	F6	22.33 ± 1.57	28.08 ± 1.428
7	F7	28.33 ± 0.59	37.89 ± 1.345
8	F8	26.00 ± 1.01	36.37 ± 1.965
9	F9	25.33 ± 0.59	34.09 ± 1.936

Table No.5: *In-vitro* disintegration time, *in vitro* dispersion time

S.No	Formulation Code	*In vitro* Disintegration Time (Sec.)	*In vitro* Dispersion Time (sec.)
1	F1	11.67 ± 2.082	20.00 ± 1.11
2	F2	09.33 ± 1.143	18.33 ± 0.56
3	F3	08.00 ± 1.023	14.33 ± 1.24
4	F4	19.30 ± 0.556	21.67 ± 0.65
5	F5	18.33 ± 0.567	19.67 ± 0.67
6	F6	16.33 ± 0.587	15.33 ± 1.25
7	F7	23.67 ± 0.556	23.67 ± 1.23
8	F8	19.33 ± 0.545	21.67 ± 0.65
9	F9	17.33 ± 0.567	20.00 ± 1.11

Table No.6: Comparative *in vitro* Dissolution study of rapidly disintegrating tablets of Clopidogrel (F1-F9)

S.No	Time (min)	Cumulative % Drug Release								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	0	0	0	0	0	0	0	0	0	0
2	3	62.65	66.04	67.24	66.22	60.22	59.04	57.26	54.96	60.11
3	6	74.49	75.98	79.00	76.97	75.53	70.26	68.53	64.65	69.91
4	9	78.72	77.16	83.21	79.15	77.70	76.45	71.25	73.86	75.65
5	12	85.80	88.85	93.99	81.41	83.99	85.20	76.98	79.55	81.50
6	15	89.83	91.10	96.20	85.11	88.71	90.44	78.26	82.26	85.31

Table No.7: Slope and Correlation (R) Values of Clopidogrel Formulation

S.No	Formulation Code	Cum. % Drug Released V/s. Time		Log Cumulative % Drug Retained V/s Time	
		Correlation coefficient	*Slope*	*Correlation coefficient*	*Slope*
1	F1	0.5080	7.741	0.9640	-0.065
2	F2	0.4620	7.810	0.9070	-0.067
3	F3	0.4510	8.071	0.9550	-0.081
4	F4	0.3910	7.677	0.9680	-0.048
5	F5	0.5150	7.659	0.9620	-0.060
6	F6	0.5870	7.575	0.9370	-0.070
7	F7	0.5480	7.244	0.9510	-0.050
8	F8	0.5910	7.078	0.9580	-0.048
9	F9	0.5710	7.542	0.9220	-0.068

Table No.8: Selected Formulations for Stability Studies F3, F6 and F9 Stored at 40^0C/75% Rh

S.No	Formulation Code	Tested after time (in days)	Hardness (kg/cm^2)	Disintegration time (sec)	Wetting time (sec)	Drug content (n=5)	% of Friability
			Mean ± SD (n=3)				
1	F3	10	3.81±0.29	09.67 ± 2.082	16.00 ± 1.12	9.825±0.148	0.1365
		20	3.81±0.30	09.33 ± 1.143	15.00 ± 0.67	9.725±0.113	0.1366
		30	3.80±0.29	09.20 ± 1.023	17.29 ± 1.55	9.825±0.067	0.1370
2	F6	10	3.74±0.29	17.30 ± 0.556	21.67 ± 0.36	9.818±0.176	0.2105
		20	3.75±0.29	17.33 ± 0.567	20.67 ± 0.55	9.718±0.031	0.2125
		30	3.76±0.29	17.55 ± 0.587	21.78 ± 1.57	9.818±0.021	0.2130
3	F9	10	2.99±0.29	18.33 ± 0.556	23.33 ± 0.59	9.773±0.148	0.4186
		20	2.98±0.29	18.55 ± 0.545	25.00 ± 1.01	9.675±0.113	0.4190
		30	2.97±0.29	18.60 ± 0.567	26.33 ± 0.59	9.976±0.054	0.4195

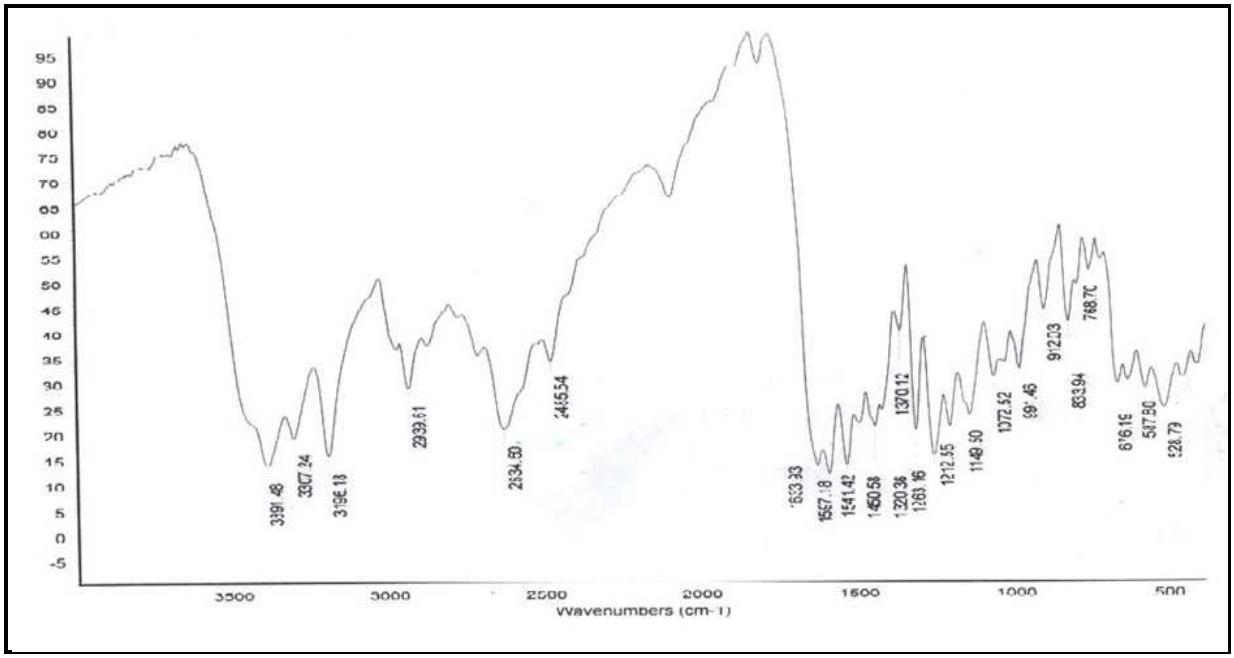

Figure No.1: I.R. Spectra of Clopidogrel

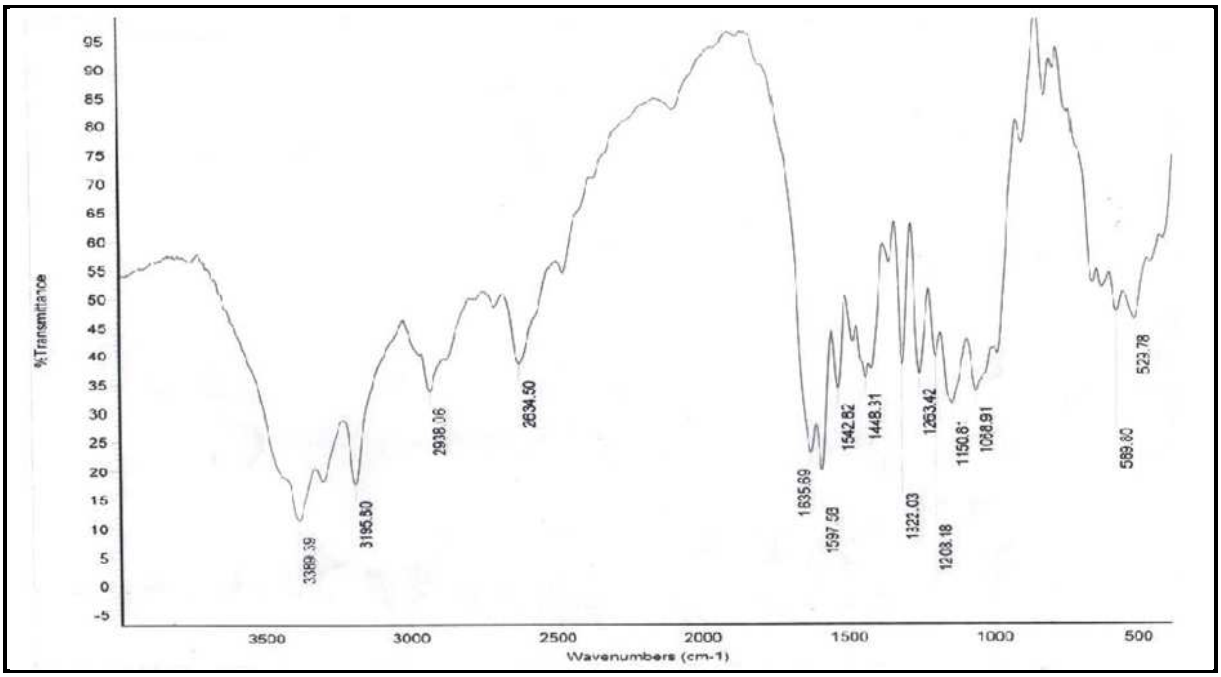

Figure No.2: I.R. Spectra of Clopidogrel + Avicel Ph 102

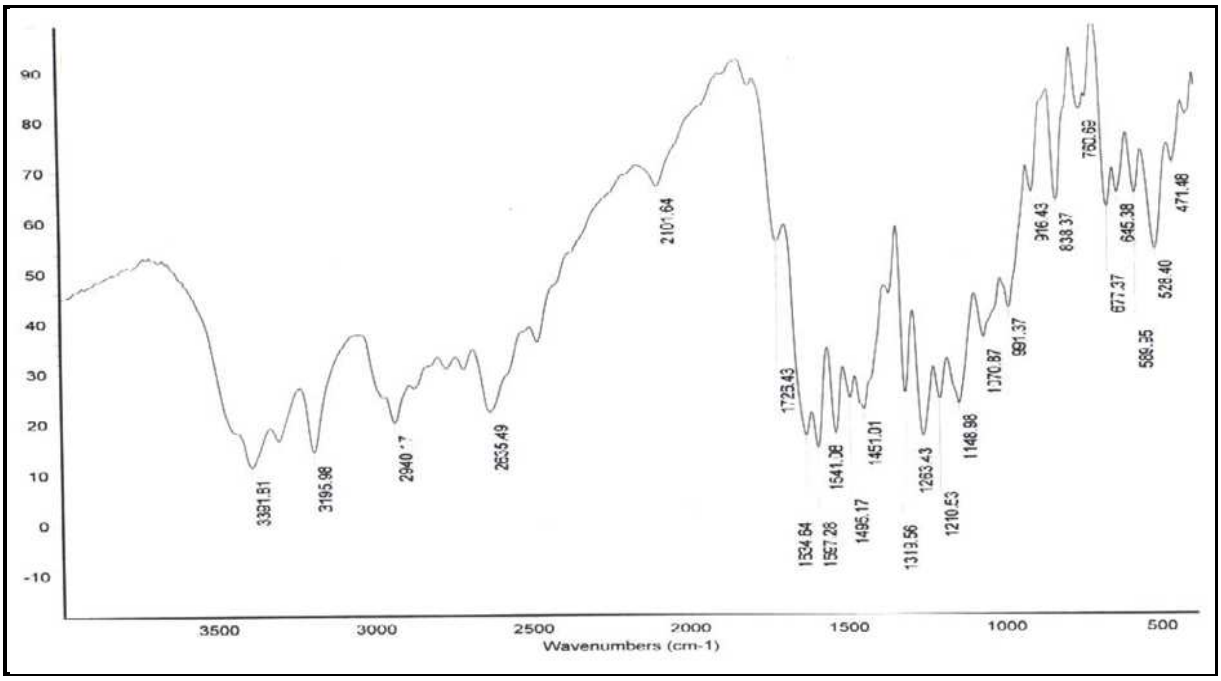

Figure No.3: I.R. Spectra of Clopidogrel + Eudragit E 100

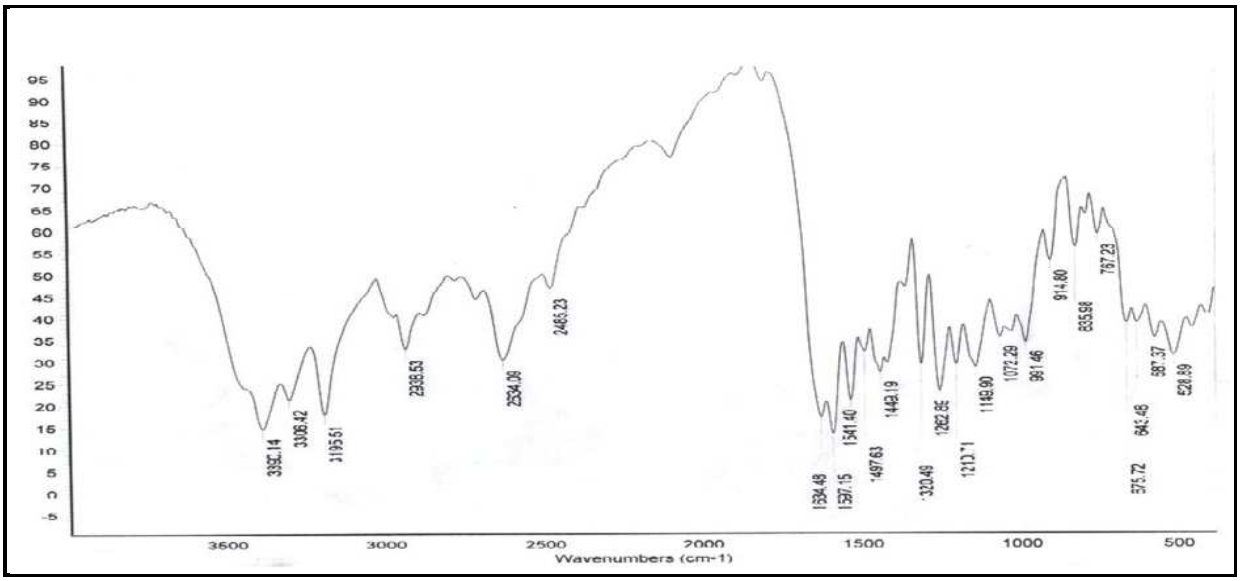

Figure No.4: I.R. Spectra of Clopidogrel + Sodium starch glycolate

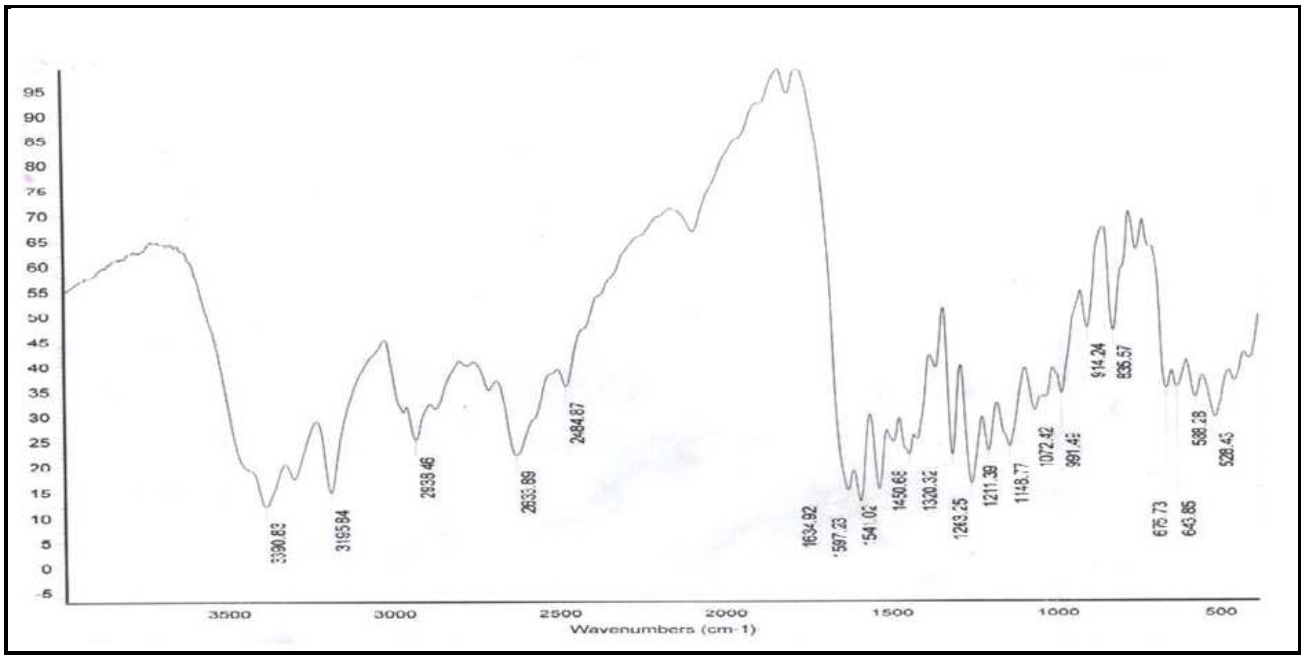

Figure No.5: I.R. Spectra of Clopidogrel + L-Hydroxy propyl cellulose

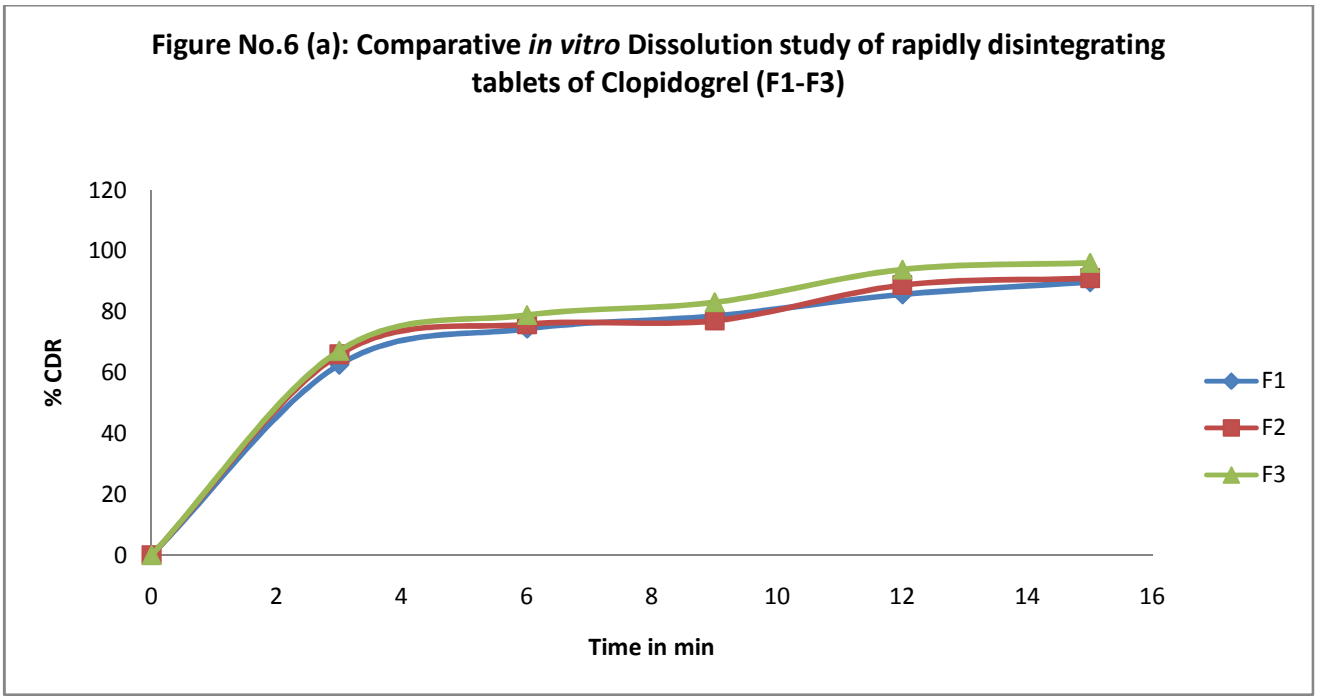

Figure No.6 (a): Comparative *in vitro* Dissolution study of rapidly disintegrating tablets of Clopidogrel (F1-F3)

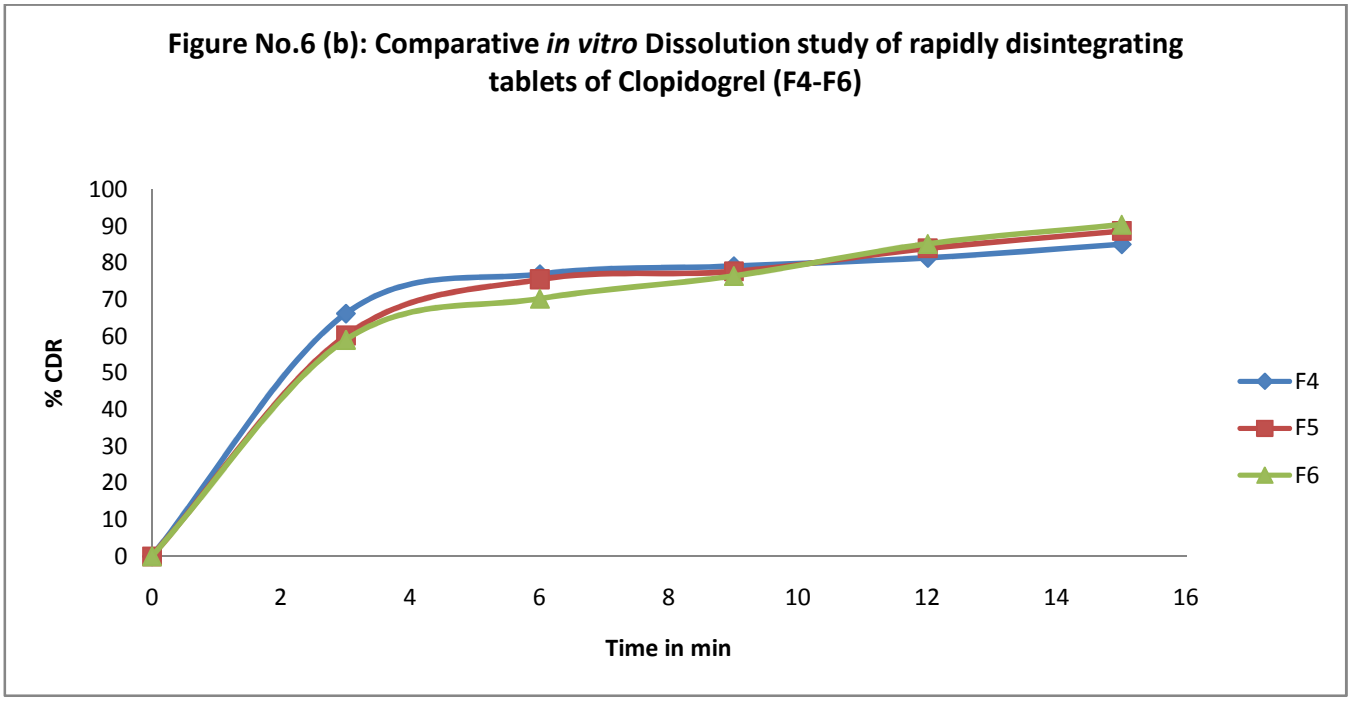

Figure No.6 (b): Comparative *in vitro* Dissolution study of rapidly disintegrating tablets of Clopidogrel (F4-F6)

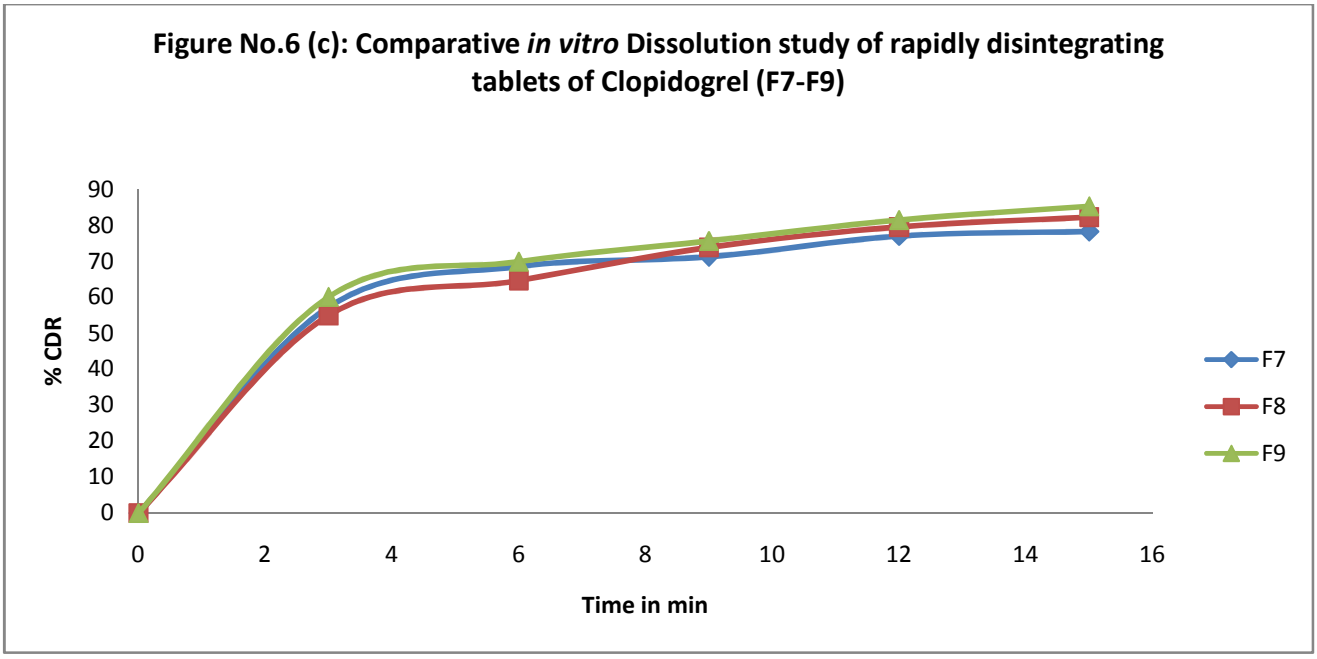

Figure No.6 (c): Comparative *in vitro* Dissolution study of rapidly disintegrating tablets of Clopidogrel (F7-F9)

CONCLUSION

Preformulation studies of Clopidogrel were performed; the FTIR analysis revealed that the super disintegrants and excipients used were compatible with Clopidogrel. Fast dissolving tablets of Clopidogrel can be prepared by Mass Extrusion technique using the different super disintegrants, namely Sodium starch glycolate, Avicel PH 102(MCC), and L-HPC. Amongst all the formulations, formulation containing sodium starch glycolate as superdisintegrants is fulfilling all the parameters satisfactorily. It has shown excellent *in vitro* disintegration, *in vitro* dispersion time, compared to other super disintegrants. Overall, formulations F3 containing Sodium starch glycolate at 10% and F6 containing Avicel PH 102 10% tablets disintegrated rapidly to release the drug. The formulations F3, F6, F9 were selected for stability studies on the basis of their better and satisfactory evaluation studies parameter. These formulations showed not much variation in any parameter even after the period of 30 days. From these results it was concluded that, formulations F3, F6, F9 are found to be stable and retained their original properties.

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