Tianjin Daxue Xuebao (Ziran Kexue yu Gongcheng Jishu Ban)/
Journal of Tianjin University Science and Technology
ISSN (Online): 0493-2137
E-Publication: Online Open Access
Vol:56 Issue:02:2023
DOI 10.17605/OSF.IO/6DZVE

FORMULATION DEVELOPMENT AND OPTIMIZATION OF PRASUGREL FINAL DOSAGE FORM BY DIRECT COMPRESSION METHOD

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Abstract

Background: Prasugrel is a member of thienopyridine class of ADP receptors that reduce the aggregation ("Clumping") of platelets by irreversibly binding to P_2Y_{12} receptors. **Objective:** The aim of this study is to develop new formulation of Prasugrel tablets by direct compression method which is simple and cost-effective manufacturing technique. **Methods:** To obtain the best optimized product by applied central composite rotatable design (CCRD) software, nine different formulations were developed. Magnesium stearate and croscarmellose sodium were taken as independent variables. Blends were examined for various evaluating parameters like apparent bulk and tapped density, compressibility index, angle of repose and lose on drying. Newly developed compressed tablets were then evaluated using pharmacopeial and non- pharmacopeial tests for physical and chemical characteristics of core tablets i.e., hardness, weight variation test, friability (%), disintegration test (min) whereas coated tablets were evaluated for weight variation, Assay and dissolution. Three different dissolution media i.e. 0.1N HCl (pH 1.2), phosphate buffer pH 4.5 and pH 6.8 were used for calculating the percentage release of Prasugrel and their release pattern was compared with innovator brand by using the model independent methods like similarity (f_2), dissimilarity (f_1) and model dependent methods like first order, Hixson Crowell method and Weibull method. Micromeritic properties of powder blends were within acceptable limits of all nine formulations. **Results:** All the physio chemical tests found satisfactory and comparable with reference product. The comparative dissolution profile results revealed that Trial-05 showed maximum similarity i.e., 71.16, 72.59 and 68.49 at three different pH dissolution media. Dissimilarity factor was also comparable in Trial 5 i.e., 2.66, 4.63 and 3.95 at 0.1HCl, buffer pH 4.5 and 6.8 respectively. Model dependent approaches showed the maximum r^2 values of Trial 5 i.e., greater than 0.900 at all three reported pH. Results also explained that model dependent comparison is best choice as compared to model impendent approaches. **Conclusion:** New formulation of Prasugrel tablets final dosage form was developed and optimized and evaluated based on physiochemical parameters which were found satisfactory. Comparative dissolution profile results revealed that drug is comparable with reference product in term of efficacy. **Highlights:** The developed formulation offers various advantages over innovator brand in terms of patient compliance as well as in terms of cost effectiveness and easy to manufacture.

INTRODUCTION

Prasugrel is a potent, orally administered third generation thienopyridine that irreversibly inhibits the platelet aggregation via binding with P2Y12 receptor. Molecular structure of

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Prasugrel is shown in Figure-1. Compared to other drugs of the same class including Ticlopidine and Clopidogrel, Prasugrel also inhibits adenosine diphosphate-induced platelet aggregation more rapidly, more consistently, and to a greater extent than do standard and higher doses of Clopidogrel in healthy volunteers and in patients with coronary artery diseases (1-2). As per a reported pharmacodynamic study, acute coronary syndrome (ACS) patient can be safely switched from Clopidogrel to Prasugrel and that doing so results in a further reduction in platelet function after one week. When patient receive a loading dose of Prasugrel prior to switching from Clopidogrel, the reduction in platelet function occurs within two hours. Prasugrel is a BCS class II drug and exhibits pH dependent solubility and it is very soluble at low pH conditions (3-4).

Most common oral dosage forms in clinics are tablets due to its convenience, accurate dosage form and better stability. The simplest and cost-effective method is direct compression method for the manufacturing of oral pharmaceutical tablets. It is always challenging to select as well as measure the proper excipient, but this problem is encountered. Tablets manufacturing with direct compression is most convenient and appreciable process. It has several advantages over other manufacturing processes which includes fewer processing stages, elimination of heat and moisture effects, highly productive and lesser cost. It also suits well for hygroscopic and thermos-sensitive substances. Furthermore, concerning the manufacturability, a good flow ability of the blend, i.e., the dry mixture of excipients and drug, is critical for the compression of the tablets in terms of dissolution, friability and content uniformity (5).

While considering pharmaceutical formulations, statistical design software possesses substantial importance. Mostly used designs are full factorial, fractional factorial, and central composite rotatable designs (CCRD) soft wares. CCRD has many advantages in the form of defined number of experiments which shows the effect of independent variables with dependent variables with the different levels, predicted values. In the study the computerized software Design expert 8 was used for the application of CCRD (6). In usual practice, the formulations are developed by changing the levels of certain variables at a time and keeping other variable constant to analyze the effect of any specific variable on this formulation. For typically solid oral dosage form containing APIs with suitable properties a comparative in vitro dissolution profile similarity & differentiation can be used to document equivalence of developed formulation in innovator drug product (7-8).

In present study, CCRD method is used to formulate different trials of Prasugrel drug by simple direct compression method. Keeping all physiochemical properties in consideration which include weight variation, friability, disintegration time, assay and dissolution was analyzed. Stability studies of tablets were conducted as per ICH guideline, Q1A (R2) which gave good support to newly developed formulation (9-10). The comparison of dissolution dependent and independent model used to further evaluate formulation equivalency with reference available product (11).

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EXPERIMENTAL

Instrumentation

a) HPLC – HPLC analysis was performed on integrated system LC-2010C (Shimadzu Corporation, Kyoto, Japan) consisted of a 4-liquid gradient system, high-speed autosampler, column oven, and UV-visible (UV-Vis) detector. Chromatograms were recorded and integrated with LC solution (Shimadzu) chromatographic PC software.

b) Dissolution apparatus – A dissolution apparatus was used (Electro Lab., India), consisted of 12 glass vessels.

c) Spectrophotometer: UV-1800 Spectrophotometer purchased from (Shimadzu, Kyoto, Japan)

d) Disintegration apparatus: A DT apparatus was used (Electro Lab., India) with 6 baskets.

e) Harness tester: A hardness tester purchased from (Pharmatest, USA).

f) Friability Tester: A Friability tester was used (Pharmatest, USA).

g) Analytical balance: Analytical weighing balance was purchased from Shimadzu, Japan.

h) Stability Chamber: Stability chamber was purchased from Thermo Lab, India.

i) Milli-Q water purification system – A Milli-Q integral 3 system mode was used (Millipore, Billerica, MA).

j) Glassware - All glassware used in analysis purchased from Pyrex (Germany).

k) Compression machine: Compression machine was used (Zentech, China) with single punch.

l) Coating machine: Glatt tabletop coater with Pan, Binzen, Germany.

Materials, Standards, Reagents and Chemicals

a) Microcrystalline cellulose PH-102 - (FMC Corporation, USA).

b) Croscarmellose sodium - (FMC Corporation, USA).

c) Magnesium stearate - (Dow chemicals, USA).

d) HPMC (E-5) - (FMC Corporation, USA).

e) Titanium dioxide - (FMC Corporation, USA).

f) Polyethylene glycol - (FMC Corporation, USA).

g) Instacoat blue - (FMC Corporation, USA).

h) Prasugrel – API and Standard – HEC pharma, Shaoguan city, China

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i) Acetonitrile – HPLC grade (Fisher scientific, USA).

j) Potassium dihydrogen phosphate – Analytical grade (Merck, Germany).

k) Sodium citrate - Analytical grade (Merck, Germany).

l) Sodium dihydrogen phosphate – Analytical grade (Merck, Germany).

m) Hydrochloric acid - Analytical grade (Merck, Germany).

n) Water – Purified in-house using the Milli-Q integral 3 system.

o) Sample – Obtained from Department of Pharmacy, University of Karachi.

Optimization of tablets formulation

To obtain optimized product, nine different formulations were prepared by using central composite design software. Croscarmellose sodium and Magnesium stearate were used as independent variables. The dependent variables were measured from friability and disintegration time tests. Percentage composition, formulation optimization design and low and high levels of variables are shown in (Tables 1 and 2) respectively.

Properties of blend powder

Micrometric tests of powder i.e. bulk and tap density, Percentage compressibility and flow properties (angle of repose) tests were performed by using simple apparatus i.e. measuring cylinder and funnels. Loss on drying was performed on IR moisture analyzer.

Preparation of tablets

All ingredients including API were accurately weighted, passed through 20 mesh sieve and mixed in pan-blender for 5 minutes and then tablets were compressed. For the preparation of coating solution, all ingredients, Hypromellose 5cps, polyethylene glycol 6000, Titanium Dioxide and Lake indigo carmine was added one by one in beaker containing purified water with temperature of 60°C-80°C in it under stirring.

Evaluation of compressed tablets

Weight variation test:

Twenty tablets were randomly selected and weighed to determine the average weight and were compared with individual tablet weight. The percentage weight variation was calculated.

Hardness:

Hardness of all 10 formulated tablets were determined and reported.

Friability test:

Friability of final tablets was determined by weighed amount of 20 tablets and subjected into rotating drum of friability test apparatus. The drum was rotated at a speed of 25 rpm for 4 minutes and reweighed the tablets. %Friability was calculated by the following formula.

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$$\text{Friability} = \frac{W_{\text{Initial}} - W_{\text{final}}}{W_{\text{initial}}} \times 100 \quad (1)$$

Disintegration time:

The test was carried out on 6 tablets using USP basket assembly, distilled water at 37°C±2°C was used as disintegration medium and the time in minutes taken for complete disintegration of the tablet with no palable mass remaining was measured in minutes (12).

Assay:

Twenty tablets from tablets formulation were randomly selected and crushed. Portion of powder was taken which containing 25mg of Prasugrel in 25ml of volumetric flask. Add 15 ml of diluent and sonicated it for 15 min with intermittent shaking. Make up the volume with diluent and mixed. Filter this solution through 0.45 micron and further dilute 5ml aliquot to 25ml volumetric flask to get final concentration of 100µg/mL solution. Prepared standard of same concentration and run HPLC system. the mobile phase containing 0.01M potassium dihydrogen phosphate pH 6.0, acetonitrile & water in the ratio of 40:54:6 (%v/v), the flow rate was 1.2 mL/min and estimation wavelength was 235nm. Inject 10µl of blank, standard & sample solution and calculate %content of Prasugrel.

Dissolution test:

Dissolution test was performed on 6 tablets by using citrate phosphate buffer pH 4.0, Apparatus was USP II (paddle), 75 rpm for 45 minutes on all nine formulations. Drug concentrations were measured by UV spectrophotometer at 235nm of wavelength (13).

Comparative dissolution study:

Test was carried out in three dissolution medium buffer pH 1.2, buffer pH 4.5 & buffer pH 6.8 (9). Dissolution parameters were applied, USP apparatus II (paddle method), rotation speed was 75 rpm, temperature of medium 37 ± 0.5ºC, samples intervals were 10, 15, 20, 30, 45 & 60 minutes by using 12 tablets of each brand. Withdrawn samples were filter using 0.45 filter. Drug concentrations were measured at 235nm of wavelength.

Model independent approach:

$$f_1 = \left[\frac{\sum_{t=1}^{n}(R_t - T_t)}{\sum_{t=1}^{n} R_t}\right] \times 100 \quad (2)$$

$$f_2 = 50 \times \log\left\{\left[1 + \left(\frac{1}{n}\right)\sum_{j-1}^{n}\left|R_j - T_j\right|^2\right]^{-0.5} \times 100\right\} \quad (3)$$

Where n is the sample number, and Rj and Tj are the percentage of the reference and test drug release, respectively, at different time intervals. If f2 of two dissolution drug release profiles is between 50 and 100, then these two drug release profiles are similar (14-15).

Model Dependent Approach:

Model dependent approaches were applied by using dissolution profile of Prasugrel release data which were First order, Hixson-Crowell and Weibull model.

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$$\ln C = \ln C_0 - kt \quad (4)$$

Where, C0 is the initial concentration of drug and K is first order constant and t is the time. Immediate release dosages followed the release rate which is not time dependent but concentration dependent

$$C_o^{1/3} - C_t^{1/3} = k_{HC}t \quad (5)$$

Where, C0 is the initial concentration of drug in tablets and the Ct is the remaining concentration of drug in the dosage form at initial time. KHC is the Hixson-Crowell constant.

$$m = 1 - \exp\left[\frac{-(t-T_i)^{\beta}}{T_d}\right] \quad (6)$$

The equation 6 repaired in the following form

$$\log[-\ln(1-m)] = \beta \log(t - T_i) - \log T_d \quad (7)$$

Where, ß is the shape parameter obtained from slope, characterize the curve as exponential (ß=1), S shaped with upward curve followed by turning points (ß>1) or parabolic with higher initial slope, after that consistent with the exponential (ß<1). T_i is the lag time, in most cases zero and Td is the time interval in which 63.2% of the drug released from the dosage form. This equation can be successfully applied in much type of immediate release dissolution curve (16).

Stability studies

The purpose of stability testing is to provide evidence on how the quality of drug product varies with time under the influence of variety of environmental factors such as temperature, humidity and light, and to establish a retest period of drug substance or a shelf life for the drug product and recommended storage condition[i]. Stability studies was conducted on newly developed product formulation at accelerated condition (40°C±2°C/75%RH±5%RH) for 6 months and testing frequency was 0,3 and 6 months and quality of product was evaluated based on available data (17).

RESULTS AND DISCUSSION

Nine formulations of Prasugrel tablets were processed with different concentration of croscarmellose sodium, microcrystalline cellulose (PH-102) and Magnesium stearate as provided in (Table-1). Microcrystalline cellulose was used as binder which is self-lubricating[ii]. Central composite design was successfully used for best combination of the excipients as shown in (Table-2). Magnesium stearate used as lubricant while Croscarmellose sodium was used as disintegrant. Bulk density, tapped density, Hausner's ratio and compressibility index of the powder blend were found within range. Values of compressibility index ranged from 12.19 to 20.16, which was considered good and passable respectively. Loss on drying test was done after taking 1g of sample from all formulated blends and the results showed direct effect of microcrystalline cellulose concentration on results. All blends evaluation results are provided in (Table-3).

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Croscarmellose sodium was used as super disintegrant at low concentrations i.e., 2-5% which also showed remarkable effect on all micromeritic properties of powder blends.

Nine compressed formulations and the reference brand Effient® were further evaluated by physicochemical tests like hardness, friability, weight variation and assay as shown in (Table 4). Gradually decrease in hardness from trial 1 to trial 3 was due to increased concentration of microcrystalline cellulose and decreased concentration of croscarmellose sodium. Weight of tablets was adjusted 100 mg for core and 103 mg for coated tablets as shown in table 5 which was under the controlled limit of ± 7.5, while actual weight of Effient (marketed brand was approx. 130mg). Presence of croscarmellose sodium showed the rapid disintegration time and low friability values i.e., 4 to 8 minutes and 0.26-0.59 % respectively which was within Pharmacopeial limits. Final formulation of tablets is provided in (Table-5). Assay results of all trial formulations and reference brand were found satisfactory with range from 97.15 to 99.89%. Physicochemical and dissolution parameters of all the trials were within limits but Trial 5 showed best results due to higher assay value i.e., 99.89% as shown in (Table-5).

Model dependent approaches like first order, Hixson Crowell and Weibull model were successfully applied and their regression values were calculated. Regression values in first order kinetics were ranged from 0.7138 to 0.9602 at pH 1.2, 0.7300 to 0.9838 at pH 4.5, 0.9083 to 0.9937 at pH 6.8 phosphate buffer solutions. Results revealed that release pattern of Prasugrel followed first order at pH 6.8 due to acidic nature and higher solubility in alkaline medium but lower values of r^2 at pH 1.2 and 4.5 showed less solubility. Values of β in case of Weibull model ranged from 0.410 to 0.743 at pH 1.2, 0.457 to 0.801 at pH 4.5 and 0.530 to 0.648 at pH 6.8 phosphate buffer due to their parabolic curve shape at initial concentrations points. Value of τ was also found less than 1 in each case as provided in (Table-6).

Model independent studies i.e., similarity factor (f_2) and dissimilarity factor (f_1) were calculated for the comparison of manufactured brands with Effient. ® Similarity values were ranged from 55.26 to 71.16 at pH 1.2, 59.04 to 72.59 at pH 4.5 and 52.18 to 68.49 at pH 6.8 buffer solutions. Trial 5 showed maximum similarity value 68.49 to 72.59 at different pH mediums due to its similar physicochemical properties with Effient as shown in Figure -2. Dissimilarity values of Trial 5 were also very low as compared to all reported formulations as shown in (Table- 7).

Stability studies of final formulation was conducted at accelerated condition (40°C±2°C/75%RH±5%RH) for 6 months and there was no any significant change found in assay and other critical parameters as shown in (Table 8).

ADVANTAGES AND APPLICATIONS

The physiochemical results for blends and final dosage form indicated that the newly developed formulation of tablets is cost effective and easy to process by using less number and ingredients and direct compression manufacturing process. Comparative dissolution profile of new final formulation is comparable with reference product.

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CONCLUSION

In the present work efforts have been made to prepare and evaluated immediate release Prasugrel tablets. Direct compression method was used due to simpler and economical manufacturing process. Blend and compressibility evaluation studies based on optimization technique revealed that the developed formulation met acceptance criteria for all critical attributes. Comparative drug release from two different brands at different buffers ranged from pH 1.2 to 6.8 are found satisfactory based on the f_2 and f_1 values obtained. Stability studies indicated that developed product was stable at accelerated conditions up to 6 months in all critical attributes. The developed formulation offers various advantages over innovator brand in terms of patient compliance as well as in terms of cost effectiveness and easy to process.

Acknowledgement:

We would like to thank University of Karachi Pharmaceutics department for their support during formulation development and analytical activities.

Funding:

All the fundings for this research were sponsored by University of Karachi.

Conflict of interest:

The authors declared that they have no conflict of interest.

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Tables:

Table 1: Composition of formulation trials Prasugrel (API take 5mg in each formulation) and Croscarmellose sodium (X1), Magnesium stearate (X2) & Avicel PH-102 (X3) compositions in formulation trials are as under

Formulations	Level of variables		%Composition of tablets			Composition of tablets (mg/tab)			Total weight (mg/tab)
	X_1	X_2	X_1	X_2	X_3	X_1	X_2	X_3	
Trial-01	1	-1	3.2	0.8	91.0	3.2	0.8	91.0	**100.0**
Trial-02	-1	1	4.8	0.8	89.4	4.8	0.8	89.4	**100.0**
Trial-03	-1	-1	4.0	1.2	89.8	4.0	1.2	89.8	**100.0**
Trial-04	1	1	4.8	1.2	89.0	4.8	1.2	89.0	**100.0**
Trial-05	0	1	4.0	1.0	90.0	4.0	1.0	90.0	**100.0**
Trial-06	0	0	3.2	1.0	90.8	3.2	1.0	90.8	**100.0**
Trial-07	0	-1	3.2	1.2	90.6	3.2	1.2	90.6	**100.0**
Trial-08	-1	0	4.8	1.0	89.2	4.8	1.0	89.2	**100.0**
Trial-09	1	0	4.0	0.8	90.2	4.0	0.8	90.2	**100.0**

Table 2: Levels of variables in optimized formulations

Serial No.	Variables	Low level	High level
1	Avicel PH-102	89.0 mg	91.0 mg
2	Croscarmellose sodium	3.2 mg	4.8 mg
3	Magnesium stearate	0.8 mg	1.2 mg

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Table 3: Results of Lubricated blend parameters

Formulations	Lubricated blend parameters					
	Angle of repose (degree)	Bulk density (g / cm$^{3)}$	Tapped density (g / cm$^{3)}$	Compressibility Index (%)	Hausner's Ratio	Loss on drying (%)
Trial-01	33.12	0.550	0.648	15.12	1.24	1.61
Trial-02	32.20	0.502	0.602	16.61	1.19	1.68
Trial-03	34.88	0.495	0.620	20.16	1.19	2.02
Trial-04	35.10	0.480	0.588	18.36	1.22	1.90
Trial-05	35.38	0.540	0.615	12.19	1.15	1.20
Trial-06	33.11	0.532	0.638	16.61	1.18	2.10
Trial-07	31.02	0.480	0.592	18.91	1.20	1.85
Trial-08	32.10	0.526	0.628	16.24	1.17	1.92
Trial-09	33.13	0.511	0.612	16.50	1.23	2.19

Table 4: Results of physiochemical test parameters

Physiochemical parameters results						
Formulations	**Weight variation (mg)**	**Hardness (kp)**	**Disintegration (min)**	**Friability (%)**	**Average % Dissolution**	**Average % Assay**
Limits	± 7.5%	≥ 4.0	< 15 mins	< 1%	> 80%	(95-105)%
Trial-01	100.33	8.2 – 13.8	5.0	0.26	88.15	99.25
Trial-02	101.15	6.8 – 9.2	7.0	0.38	91.28	97.15
Trial-03	100.96	5.0 - 7.3	7.0	0.38	93.63	99.25
Trial-04	100.10	6.2 – 9.8	6.0	0.40	94.12	98.36
Trial-05	100.20	7.2 – 10.9	6.0	0.52	97.12	99.89
Trial-06	99.36	5.5 – 10.2	7.0	0.35	96.63	97.63
Trial-07	101.78	8.0 – 12.9	7.0	0.26	94.15	98.58
Trial-08	102.01	8.9 – 13.0	8.0	0.39	91.28	99.60
Trial-09	99.58	7.0 – 13.8	4.0	0.58	93.12	99.10
Innovator brand	130.0	6.5 - 9.0	4.0	0.55	96.58	99.36

Table 5: Formulation of final coated tablets

S.No.	Ingredients	Weight (mg/tab)
1	Prasugrel	5.0
2	Avicel PH 102	90.0
3	Croscarmellose sodium	4.0
4	Magnesium stearate	1.0
Total weight (core tablet)		100.0
Coating material		
5	Methocil E-5 (HPMC)	1.85
6	Titanium dioxide	0.56
7	Polyethylene glycol	0.56
8	Instacoat blue	0.03
Total weight (coated tablet)		103.0

Tianjin Daxue Xuebao (Ziran Kexue yu Gongcheng Jishu Ban)/
Journal of Tianjin University Science and Technology
ISSN (Online): 0493-2137
E-Publication: Online Open Access
Vol:56 Issue:02:2023
DOI 10.17605/OSF.IO/6DZVE

Table 6: Model Dependent methods for the comparison of reference and formulated products

Description of batches	First Order		Weibull model		Hixson-Crowell	
pH 1.2						
	R^2	K	β	τ	R^2	K
Innovator	0.9228	0.014	0.555	6.612	0.8446	0.004
Trial 1	0.9504	0.013	0.642	6.630	0.9029	0.004
Trial 2	0.8084	0.011	0.468	8.731	0.6985	0.003
Trial 3	0.7138	0.012	0.418	9.039	0.5676	0.003
Trial 4	0.8819	0.013	0.534	7.548	0.7863	0.003
Trial 5	0.7612	0.012	0.410	8.851	0.6302	0.004
Trial 6	0.7860	0.013	0.588	9.093	0.8432	0.003
Trial 7	0.7643	0.013	0.443	8.946	0.6587	0.004
Trial 8	0.7911	0.012	0.473	8.180	0.6300	0.004
Trial 9	0.9602	0.014	0.743	2.685	0.9053	0.003
PH 4.5						
Innovator	0.9556	0.011	0.601	0.125	0.9713	0.003
Trial 1	0.9838	0.009	0.801	2.463	0.9493	0.002
Trial 2	0.8572	0.008	0.525	3.929	0.7973	0.002
Trial 3	0.7300	0.008	0.457	8.136	0.6441	0.002
Trial 4	0.8807	0.008	0.563	7.013	0.8251	0.002
Trial 5	0.7235	0.009	0.472	7.960	0.8872	0.002
Trial 6	0.8598	0.0012	0.531	7.502	0.7693	0.002
Trial 7	0.8598	0.008	0.503	7.307	0.7306	0.002
Trial 8	0.8080	0.009	0.540	7.451	0.7954	0.002
Trial 9	0.8593	0.008	0.744	6.523	0.9749	0.003
pH 6.8						
Innovator	0.9487	0.030	0.611	0.524	0.8594	0.008
Trial 1	0.9540	0.029	0.628	5.792	0.8754	0.008
Trial 2	0.9164	0.030	0.549	6.367	0.8116	0.008
Trial 3	0.9335	0.031	0.608	4.829	0.8393	0.008
Trial 4	0.9937	0.031	0.555	5.325	0.7737	0.009
Trial 5	0.9411	0.031	0.648	3.778	0.8512	0.009
Trial 6	0.9510	0.031	0.641	5.110	0.8866	0.009
Trial 7	0.9083	0.030	0.530	6.602	0.7981	0.009
Trial 8	0.9375	0.031	0.593	5.766	0.8148	0.009
Trial 9	0.9280	0.030	0.560	6.146	0.8271	0.009

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Table 7: Model independent comparison with innovator product (Effient)

Trial batches description	f_1 (Dissimilarity)	f_2(Similarity)
pH 1.2		
Trial 1	4.51	70.55
Trial 2	9.77	55.26
Trial 3	7.20	61.49
Trial 4	8.72	57.34
Trial 5	2.66	71.16
Trial 6	7.49	60.04
Trial 7	5.70	65.07
Trial 8	4.46	69.49
Trial 9	4.49	70.13
pH 4.5		
Trial 1	4.22	71.35
Trial 2	8.11	59.04
Trial 3	5.19	66.98
Trial 4	6.13	64.55
Trial 5	4.63	72.59
Trial 6	4.80	68.65
Trial 7	4.66	70.59
Trial 8	4.27	72.46
Trial 9	5.71	66.65
pH 6.8		
Trial 1	5.71	64.64
Trial 2	10.66	52.18
Trial 3	4.96	67.01
Trial 4	5.91	62.62
Trial 5	3.95	68.49
Trial 6	4.60	67.52
Trial 7	5.36	63.56
Trial 8	4.17	68.43
Trial 9	4.26	68.26

Table 8: Stability studies of developed product at accelerated condition (40°C±2°C/75%RH±5%RH) for 6 months

S.No.	Parameters	Specifications	Initial	3 months	6 months
1	**Appearance**	Yellow colored round shaped tablet plain from both sides	Complies	Complies	Complies
2	**DT**	<15 mins	6	5	6
3	**Hardness**	**≥**4 kp	7.0	6.8	7.2
4	**%Dissolution**	>80%	99.38	99.10	96.52
5	**%Assay**	(95 – 105)%	101.68	100.13	101.49

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Figures

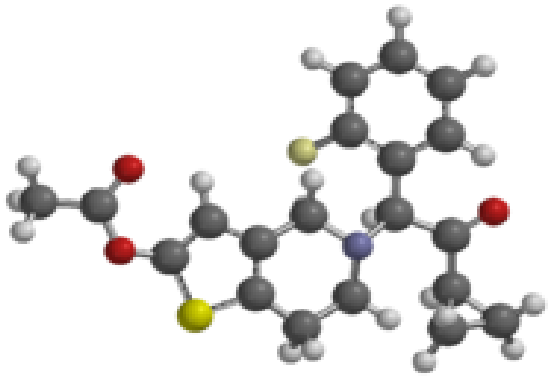

Figure 1: Molecular structure of Prasugrel

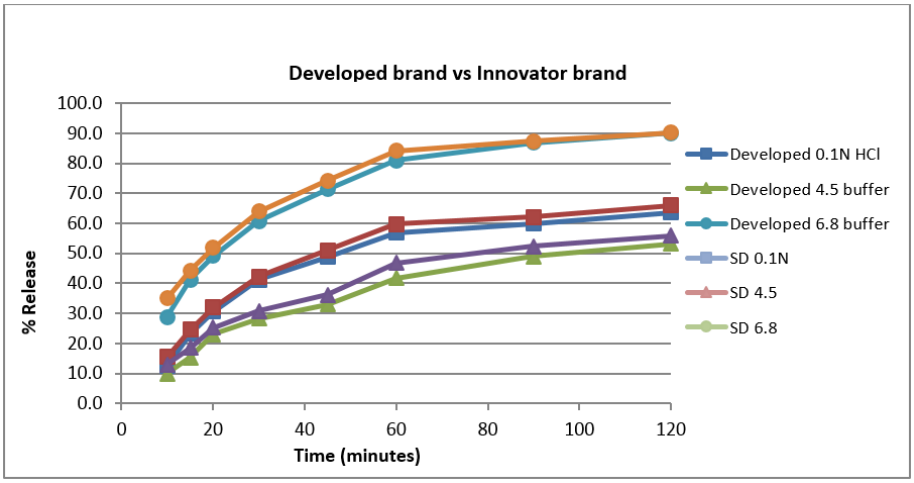

Figure 2: Graphical comparison of Prasugrel 5mg tablets VS innovator brand in pH 1.2 (0.1N HCl), buffer pH 4.5 & pH 6.8