ORIGINAL ARTICLE

In Vitro Assessment and Application of Kinetics Models on Dissolution Profile of Several Brands of Clopidogrel (75Mg) Available in Karachi, Pakistan

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ABSTRACT

Objective: This investigation focuses on conducting a comprehensive in vitro standard evaluation of ten different Clopidogrel (75mg) brands available in Karachi, Pakistan.
Methodology: The study involved pharmacopoeial tests on ten Clopidogrel tablet brands, including weight variation, friability, disintegration, dissolution, and assay. Non-pharmacopoeial tests measured thickness, diameter, and hardness. Model-dependent approaches used first-order kinetics, Higuchi, Hixson Crowell, and Weibull models. Model-independent approaches calculated the difference (f1) and similarity (f2) factors for dissolution data analysis.
Results: The average weight variation of all ten coded Clopidogrel brands fell within the USP specification of ±7.5% deviation (225.9-356.1 mg). Measurements of hardness, thickness, and diameter met specified limits outlined by USP. Disintegration times of 2-8 minutes complied with the USP standard for film-coated tablets. Friability ranged from 0.02% to 0.3%, within the standard limit, indicating tablets' sufficient mechanical strength. Assay studies revealed Clopidogrel content within the range of 98.7% to 101.30%, aligning with USP assay monograph limits. Multiple point dissolution studies in 0.1N HCl showed drug release ranging from 90.9% to 99.8%, meeting USP specifications. Similarity factor (f1) and dissimilarity factor (f2) values were within limits, reinforcing bioequivalence. Kinetic models, including first order, Hixon and Crowell were applied, and all coded brands demonstrated acceptable r2 values.
Conclusion: The study successfully implemented pharmacopeial and non-pharmacopeial tests on ten Clopidogrel (75mg) brands available in Karachi, Pakistan, demonstrating compliance with USP specifications. While the results suggest the suitability of these formulations for therapeutic use, a larger-scale study is recommended for further validation and understanding.

Key Words: Comparison, in vitro, kinetics approaches, model dependent

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INTRODUCTION

In-vitro testing encompasses all activities aimed at gathering additional information and data about any product. This information is crucial for product improvement and the establishment of regulations and standards[1]. The manufacturing processes of pharmaceuticals significantly affect the quality of the product's. One crucial technique for determining product acceptability is "dissolution testing," which evaluates a drug product's lot-to-lot quality and guides the development of new formulations[2].

Tablets, as a dosage form, are generally more stable than other forms, such as liquids, and have a longer shelf life, making them easier to store and transport[3]. Clopidogrel, a thienopyridine, falls within the category of substances that have low solubility/high permeability according to bio pharmaceutics classification. Due to its low water solubility, Clopidogrel exhibits a relatively low oral bioavailability (less than 50%) and is activated by enzymes, particularly CYP2C19 and CYP3A4 enzymes[4-6].

In this context, the study focuses on the assessment of various formulations of Clopidogrel (75mg) available

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in the market in Karachi, Pakistan. The tablets' physical attributes, such as weight variation, hardness, thickness, diameter, friability, and disintegration time, are examined to ensure compliance with pharmacopeial standards. Additionally, multiple-point dissolution studies are conducted to evaluate the kinetics of drug release from the formulations.

The growing number of formulations in the market emphasizes the need for rigorous quality control measures, comparing each product against standards outlined in Pharmacopoeia. Tablets must possess sufficient mechanical strength to withstand handling, storage, and transport, while also ensuring consistent drug release in the gastrointestinal tract[7,8]. The study introduces ten designed formulations evaluated for various parameters, including hardness, friability, thickness, assay, wetting time, disintegration time, and in-vitro drug release. The primary objective is to conduct pharmacopeial and non-pharmacopeial tests on several brands of Clopidogrel available in Pakistan nationally and apply various kinetic models to assess the multiple-point dissolution profile of Clopidogrel film coated tablets of (75mg).

METHODOLOGY

Ten products of Clopidogrel USP 75mg brands were randomly selected from the local market in Karachi, Pakistan, and each was assigned a unique identification code (C1, C2, and C3…C10). This study donot involve any human or animal studies therefore ethical review from IRB is exempted.

*Software used***:** Microsoft Excel 2016 was employed for data analysis, while the dissolution profile evaluation and application of kinetic models were conducted using the DD Solver add-in programme**.**

Instruments and Reagents: The study utilized the following equipment: Vernier Caliper (Seiko, China), Friability Tester (Curio FB 2020, Pakistan), Digital Hardness Tester, USP Basket Rack Assembly (DA 6D, Veego, India), USP Type 2 Paddle Dissolution Apparatus (Curio, Pakistan), UV Spectrophotometer (Shimadzu, Japan), Analytical balance (Shimadzu, Japan). Additionally, hydrochloric acid and distilled water were used as reagents.

Pharmacopoeial tests

Weight variation test: To initiate the weight variation test, ten Clopidogrel tablets from each of the ten brands were individually and randomly selected for weighing. The tablets were carefully chosen to ensure a representative sample. This average weight was then compared with the specific weight of each tablet to identify any variations. The estimation of weight variation was determined using the formula:

Weight Variation = (Individual weight-average weight) x 100/ average weight **(Table 1)**

Table 1: Limits of weight variation according to USP

Mean weight of tablet	Percentage difference
<130mg	±10%
>130mg and < 324mg	±7.5%
>324mg	±5%

The test criteria state that if no tablet deviates by more than twice the specified percentage limit, and no more than two tablets exceed the designated percentage, the tablet passes the weight variation test[9,10].

Friability: The friability test for tablets was conducted using a Roche friabilitor. Ten tablets were selected, and their initial weights were collectively recorded. Subsequently, these tablets were placed in the friabilitor and rotated at 25 revolutions per minute (rpm) for a duration of 4 minutes. Upon completion of the test, the same ten tablets were removed, and their final weights were recorded. This procedure was repeated for tablets from other coded brands. Friability was determined using the following formula:

$$\%F = (1\text{-}W/W0) \times 100\ \%$$

Friability of tablets <1% are treated as satisfactory11.

Disintegration Test: The disintegration test is a crucial evaluation, providing insights into the tablet's ability to break down into smaller particles, facilitating proper absorption of the drug. Adherence to the disintegration time limit is essential for ensuring the efficacy and quality of the tablets. Six tablets were chosen from each coded brand to assess their disintegration properties. For the test, each tablet was placed within an open-ended tube on a wire mesh fixed at one of its ends[6]. One tablet was introduced into each of the six tubes comprising the assembly for the coded brand. The test was conducted using distilled water at a temperature of 37 ± 2°C, and the duration of the test was set at 15 minutes.

Upon complete disintegration of the tablets, the time was meticulously noted. It is worth mentioning that, according to the United States Pharmacopeia (USP) guidelines, the disintegration time should not exceed 15 minutes for tablets to meet the specified standards[12]. This procedure was replicated for tablets from other coded brands, including C2, C3, C4…..C10.

Dissolution: The dissolution test was conducted using a USP Type II dissolution apparatus operating at 50 rpm. The dissolution medium for Clopidogrel comprised

0.1N HCl. Samples were withdrawn at specific time intervals, including 5 minutes, 10 minutes, 15 minutes, 20 minutes, 25 minutes, and 30 minutes. To maintain sink conditions, 10ml of freshly prepared 0.1 N HCl was added each time a sample was withdrawn.

The absorbance of each sample at the designated time points was measured using a UV spectrophotometer at a wavelength of 270nm, with 0.1N HCl serving as the blank. This rigorous testing protocol ensures accurate monitoring of the drug dissolution profile, crucial for assessing the tablet's performance and adherence to dissolution specifications.

Assay: The assay test was conducted using a 0.1N HCl solution. One tablet was placed in a 50ml volumetric flask containing 0.1N HCl. The mixture was sonicated for 5 minutes, followed by the transfer of 5ml of the solution into another 50ml volumetric flask. This was then diluted to 0.1N HCl, and sufficient volume was added to achieve the required total volume.

Subsequently, the solution was passed through a 0.45um filter, discarding the initial 5ml. The absorbance of the filtered solution was measured using a UV spectrophotometer at 270nm. This entire process was repeated for all selected Clopidogrel brands. The obtained results were then compared to assess the uniformity of content against the established standard. This meticulous assay test ensures accurate determination of the drug content, a critical parameter for evaluating the quality and consistency of the tablets.

Non-pharmacopoeial tests

Thickness and diameter: Non-pharmacopoeial tests were conducted to assess tablet characteristics, specifically thickness and diameter. Vernier calipers were employed for precise measurements. Ten tablets from each brand were individually measured by sliding them between the jaws of the Vernier calipers. It is essential to note that the tablet thickness should fall within a ±5% variation of a standard value, ensuring compliance with quality standards[13]. These non-pharmacopoeial tests provide valuable insights into tablet properties, and the obtained measurements were meticulously recorded and analyzed using Microsoft Excel 2019 for comprehensive evaluation and comparison among different tablet brands.

Hardness: Tablet hardness is a crucial parameter guiding both product development and quality control. Ten tablets from each product were individually tested using a digital hardness tester, and their hardness values were recorded. The acceptable range for hardness is set between 4 to 10 kg.

Model Dependent Approach

First order kinetics model: This model illustrates the absorption and elimination characteristics of the compound. First-order kinetic reactions are concentration-dependent, with higher concentrations resulting in greater elimination per unit time. Q0 and Qt represent the initial dosage form quantity and the amount released at time t, respectively.

$$\text{Log } Q = \text{Log} Q_0 - \frac{kt}{2.303} \qquad (2)$$

Here,
t = time
K = First Order Rate constant

Higuchi model: This model illustrates the release mechanism of a drug from tablet matrices and is applicable to porous systems. It establishes a direct proportionality between the total amount of drug release and the square root of the time period.

Here
K_{HZ} represents Higuchi constant

$$Q = kt^{\frac{1}{2}} \qquad (3)$$

Hixson Crowell model: This model expresses the change in diameter and surface area during drug release of tablet. It depicts the dissolution rate as a function of time for a decrease in surface area of solid.

$$Q_0^{1/3} - Q_t^{1/3} = K_{HC} \times t \qquad (4)$$

Here,
K_{HC} represents Hixson–Crowell Rate constant

Weibull model: This model is presented to compare drug release profile of matrix system. It is also useful in comparing release patterns of matrix system.

Weibull model described for different dissolution mechanisms.

$$m = 1 - \exp\left[-\frac{(t-Ti)^{\beta}}{\alpha}\right] \qquad (5)$$

M = drug's dissolution rate as a function of time t
M0 = entire quantity of dug released
T = lag time
Eq.5 cab be written as:

$$\text{Log}[-\ln(1-m)] = b \log(t - Ti) - \log\alpha \qquad (6)$$

Model Independent Approaches: The following

formulas will be used to get the dissolution data's difference factor (f1) and similarity factor (f2).

$$f_1 = \left[\frac{\sum_{t=1}^{n}(R_t - T_t)}{\sum_{t=1}^{n} R_t}\right] \times 10_0 \quad (7)$$

$$f_2 = 50 \times \log\left\{\left[1 + \left(\frac{1}{N}\right)\sum(Ri - Ti)^2\right]^{-0.5}\right\} \times 10_0 \quad (8)$$

n = number of samples
Rt = per cent release of the reference drug
Tt = per cent release of test drug
The Limit of Difference factor (f1) is between 0 and 15, while the Similarity factor (f2) is between 50 and 100.

RESULTS

DISCUSSION

This study aimed to assess different brands of 75 mg clopidogrel available in Karachi, Pakistan, focusing on parameters crucial for good manufacturing practice, such as tablet size and dosage uniformity[14]. According to the USP, for tablets weighing more than 130 mg, the mean weight variation should be within ±7.5%, with not more than two tablets deviating from the average weight, as indicated in Table 1.

The average weight of clopidogrel tablets in this study ranged from 225.9 to 356.1 mg, as presented in Table 2[15]. Hardness is a key parameter indicating the force required to break a tablet, influencing handling, dissolution, and disintegration. USP recommends tablet hardness between 4 to 10 kg[16]. The tablets in our study exhibited hardness in the range of 4.967 to 6.63 kg, ensuring sufficient mechanical strength. Using Vernier

Table 2: Pharmacopoeial and non - Pharmacopoeial Test for Clopidogrel (75mg)

S.No	Formulation Codes	Weight (mg) Mean ± SD	Thickness (mm) Mean ± SD	Diameter (mm) Mean ± SD	Hardness (kg) Mean ± SD	Friability (%)	Disintegration Time (minutes) (not >15 minutes)
1	C1	287.5±3.930	4.82±0.04	9.8975±0.06	5.465±0.24	0.10	4 minutes 22 seconds
2	C2	306.3±3.226	3.545±0.15	9.8±0.03	5.802±0.65	0.16	2 minutes 22 seconds
3	C3	319.7±3.067	4.38±0.04	10.35±0.05	5.192±0.34	0.09	2 minutes 57 seconds
4	C4	309.9±4.805	1.85±0.04	10±0.06	5.63±0.41	0.03	6 minutes 8 seconds
5	C5	225.9±2.3	3.64±0.08	8.925±0.04	6.63±0.77	0.3	4 minutes 8 seconds
6	C6	350.8±5.582	4.905±0.01	10.075±0.04	4.967±0.56	0.02	3 minutes 45 seconds
7	C7	251.3±5.367	3.625±0.34	9.075±0.04	5.215±0.34	0.03	8 minutes
8	C8	258.7±2.794	4.105±0.01	8.825±0.04	5.192±0.97	0.07	6 minutes 50 seconds
9	C9	356.1±6.518	3.32±0.071	10.5±0.08	6.337±1.067	0.02	7 minutes20 seconds
10	C10	291.2±2.785	3.3±0.01	9.925±0.04	5.577±0.041	0.03	2 minutes 1 seconds

Table 3: Assay Test of Clopidogrel (75mg)

No. of Tablets	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10
10	99.80%	100.10%	99.60%	101.20%	100.40%	99.90%	101.40%	98.70%	101.90%	100.20%
10	99.60%	101.20%	100.20%	100.40%	100.10%	98.70%	101.10%	99.60%	101.10%	100.10%
10	100.10%	99.90%	101.40%	99.90%	99.50%	99.90%	101.40%	99.60%	99.60%	99.60%
MEAN	99.83%	100.40%	100.40%	100.50%	100.00%	99.50%	101.30%	99.30%	100.87%	99.97%
SD	±0.002	±0.005	±0.007	±0.005	±0.003	±0.005	±0.001	±0.004	±0.009	±0.002

Table 4: f1 and f2 Tests with Reference Formulation C7

Similarity *(f2)* and Dissimilarity *(f1)* factor at 0.1N HCl	C1	C2	C3	C4	C5	C6	C8	C9	C10
f1 difference factor	9	4	6	6	6	6	5	7	8
f2 similarity factor	61	74	66	67	67	69	70	66	63

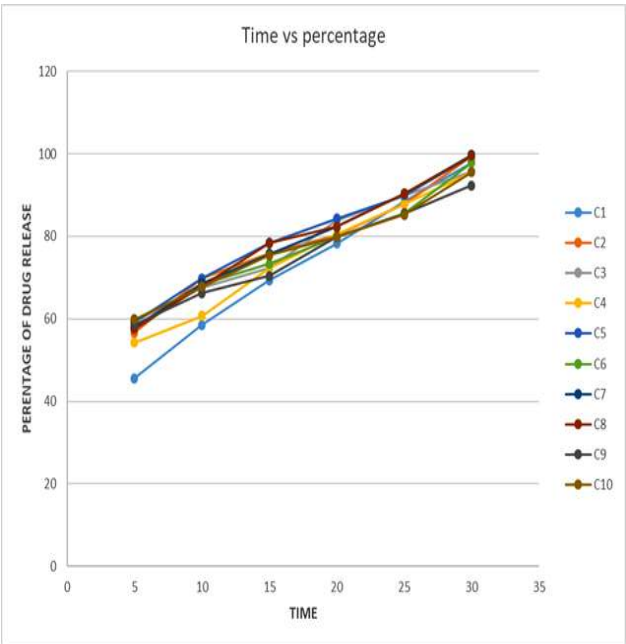

Figure 1: Graphical Presentation of Multiple Point Dissolution Studies of Clopidogrel 75mg at 0.1N HCL.

USP standard (90.0% to 110.0%), ranging from 98.7% to 101.30% (Table 3). The In-vitro Dissolution method is becoming an increasingly valuable tool for predicting bioavailability, often replacing expensive in vivo clinical research to demonstrate bioequivalence. It stands as one of the most crucial quality control tests for pharmaceutical dosage forms[20]. In this study, we examined ten different brands of Clopidogrel for dissolution in 0.1N HCl. For each brand, ten milliliters of sample were drawn at multiple time points (5, 10, 15, 20, 25, and 30 minutes) during the dissolution of 75 mg Clopidogrel tablets. The percentage of drug release was analyzed using a UV spectrophotometer at a wavelength of 270nm, with 0.1 N HCl as the blank. Figure 1 illustrates the graphical presentation of drug release at these multiple time intervals in 0.1 N HCL. At the 30-minute mark, the drug release from tablets of all selected brands was within the specified limit of the USP (not less than 80% in 30 minutes), ranging from 90.9% to 99.8%. In the past Clopidogrel quality test were conducted depending

Table 5: Release Kinetics of Coded Tablets of Clopidogrel (75mg)

Coded Tablets	First Order		Higuchi		Hixon Crowell		Weibull Model		
	r^2	k1(m)	r^2	kH(m-1/2)	r^2	kHC(m-1/3)	r^2	B	A
C1	0.9720	0.064	0.9779	15.692	0.957	0.018	0.9727	0.967	14.235
C2	0.9038	0.070	0.9395	16.558	0.9234	0.019	0.9055	1.058	16.841
C3	0.9005	0.067	0.9328	16.221	0.9133	0.018	0.9009	1.027	16.098
C4	0.9062	0.068	0.9368	16.281	0.9163	0.018	0.9065	1.023	15.753
C5	0.9033	0.068	0.9365	16.270	0.9139	0.018	0.9035	1.020	15.622
C6	0.9240	0.068	0.9537	16.291	0.9289	0.019	0.9240	1.007	14.953
C7	0.9162	0.077	0.9656	17.217	0.9216	0.021	0.9162	1.006	13.206
C8	0.9638	0.085	0.9942	17.807	0.9482	0.023	0.9639	0.986	11.289
C9	0.9864	0.083	0.9875	17.409	0.9279	0.022	0.9948	0.899	9.194
C10	0.9741	0.089	0.9699	17.819	0.9126	0.023	0.9817	0.903	8.759

calipers, we measured the thickness and diameter of ten clopidogrel brands, finding standard deviations within ±5% deviation, as shown in Table 2. For film-coated tablets, disintegration time is crucial, ensuring uniformity across batches and consistent bioavailability[17]. In our study, disintegration times ranged from 2 to 8 minutes, well below the USP standard of 15 minutes. The friability test assessed how well tablets withstand mechanical shocks and attrition during production, packaging, and shipping. USP recommends friability less than 1%, and our study revealed friability between 0.02% to 0.3%[18,19]. The assay test, evaluating API content in pharmaceutical tablets, showed that all Clopidogrel brands met the on USP Pharmacopeia. Various kinetic models, including first order, Higuchi, Hixon Crowell, and Weibull models, were applied to the Clopidogrel dissolution data[21]. First-order kinetics leverages the concepts of absorption and elimination to describe the behaviour of a molecular entity[22]. The Higuchi model, suitable for porous systems, elucidates the drug release mechanism from tablets[23]. The Hixon Crowell model describes changes in surface area and diameter of tablets during drug release[21]. The Weibull kinetic model presents different types of drug release behaviours and is useful for contrasting release patterns of various matrix systems[24]. To measure the similarity between dissolution profiles, factors f1 and f2 were employed.

The Limits of Difference factor (f1) ranges between 0 and 15, while the Similarity factor (f2) ranges between 50 and 100. In this study, f1 and f2 values were calculated using the C7 reference standard, selected based on drug release. All brands showed f1 and f2 values within the acceptable limits, as presented in Table 4. Equations 2, 3, 4, 5, and 6 were utilized to compute model-dependent techniques, including First order, Higuchi model, Hixon Crowell model, and Weibull model, using a dissolution data solver and add-in programme in Microsoft Excel 2016. All kinetic models were evaluated based on the r^2 statistic for tablets designated C1–C10, as detailed in Table 5.

CONCLUSION

This comprehensive study aimed to assess the pharmaceutical quality and dissolution behaviour of various brands of 75 mg Clopidogrel tablets available in the local market of Karachi, Pakistan. The investigation covered a range of pharmacopoeial and non-pharmacopoeial tests, including weight variation, hardness, friability, disintegration time, thickness, diameter, assay, and dissolution studies. The tablets demonstrated satisfactory weight uniformity, mechanical strength, and resistance to friability, meeting pharmacopoeial standards. Disintegration times were well within the specified limits, ensuring prompt drug release in the gastrointestinal tract. The assay results indicated that the tablets contained the active pharmaceutical ingredient within the acceptable range, confirming the potency of the formulations. The dissolution studies, conducted in 0.1N HCl at various time intervals, revealed consistent drug release profiles for all brands. At the 30-minute mark, the drug release from all tested brands was within the USP-specified limits (not less than 80% in 30 minutes), ranging from 90.9% to 99.8%. Additionally, various kinetic models, including first order, Higuchi, Hixon Crowell, and Weibull models, were applied to the dissolution data, providing insights into the drug release mechanism but it was observed that clopidogrel release mechanism follows first order kinetics and Hixon Crowell cube root law Furthermore, model-independent approaches, utilizing factors f1 and f2, demonstrated similarity between dissolution profiles, reinforcing the quality and bioequivalence of the tested formulations. The values of f1 and f2, obtained with the reference standard C7, fell within the acceptable ranges. This research successfully integrated pharmacopoeial and non-pharmacopoeial assessments, dissolution studies, and kinetic modeling to comprehensively evaluate the quality and performance of different Clopidogrel formulations. The results affirm the suitability of these formulations for therapeutic use and contribute valuable data for regulatory compliance and pharmaceutical quality assurance[19]. The methodology employed, including the application of various kinetic models, enhances our understanding of drug release mechanisms, supporting further advancements in pharmaceutical research and development.

Conflict of interest: The authors declare no conflict of interest.

Authors' Contribution: HA and KZA: worked on Conceptualization, Financial support and guidance, HB: worked on Introduction, AS: worked on Methodology, WR: Worked on Results and NM: Worked on Discussion.

REFERENCES

1. Galata DL, Zsiros B, Mészáros LA, Nagy B, Szabó E, Farkas A, Nagy ZK. Raman mapping-based non-destructive dissolution prediction of sustained-release tablets. J Pharm Biomed Anal. 2022 Apr 1;212:114661
2. Prabu SL, Suriyaprakash T, Thirumurugan R, Shanmugarathinam AJPT. Process validation: A review. Pharma times 2014;46(4):12-5.
3. Bhavana P, Reddy MSJGB, Sciences P. A review on co-processed excipients used in direct compression of tablet dosage form. Bio and Pharma Sci. 2023;23(1):212-9.
4. Rao KR, Lakshmi KR. Design, development and evaluation of clopidogrel bisulfate floating tablets. Int J Pharm Investig. 2014;4(1):19-26.
5. Lo ST, Li RHL, Georges CJ, Nguyen N, Chen CK, Stuhlmann C, et.al. Synergistic inhibitory effects of clopidogrel and rivaroxaban on platelet function and platelet-dependent thrombin generation in cats. J Vet Intern Med. 2023;37(4):1390-1400
6. Abdul-hasan MT, Al-shaibani AJ, Wannas AN, Hasan al-gburi KM. Quality control testing of conventional clopidogrel bisulfate tablets marketed in Iraq. Int J App Pharm. 2022 7;14(1):221-5.
7. Al-Saikhan F, Ahmad N, Abd-Elaziz M, Iqbal MS. Adverse Effects of Clopidogrel: a Cross Sectional Study of the FDA Adverse Event Reporting System Database. Lat. Am. J. Pharm. 2022;41(7):1388-91.
8. Iqubal MK, Singh P, Shuaib M, Iqubal A, Singh MJ, Devel. Recent advances in direct compression technique for pharmaceutical tablet formulation. Int J of Pharma Res and Dev.2014 ;6(1):49-57.
9. Gunda RK, Kumar JN. Formulation development and evaluation of amisulpride fast dissolving tablets. J.Pharm. Sci 2018;43(2):105-16.
10. Dasari T, Kala SLJ, Nadendla RR. In process quality control tests of solid dosage forms: a comprehensive review. sch Acad J of Pharm 2017;6(8):334-45.

11. Osei-Yeboah F, Sun CC. Validation and applications of an expedited tablet friability method. Int J Pharm. 2015;484(1-2):146-55.

12. Markl D, Zeitler JA. A Review of Disintegration Mechanisms and Measurement Techniques. Pharm Res. 2017;34(5):890-917

13. Kumar D, Singh J, Antil M, Kumar VJ, Sciences B. Quality control of tablets: a review. Int. J of Uni Pharm and Bio sci 2016;5(4):53-167.

14. Mahammed N, Yadav H, Thulluru A, Narayana N, Saravanakumar A, Balaji S, et al. Formulation and evaluation of clopidogrel bisulphate tablets by liquisolid compact technique. Res J Pharm & Technol. 2020;13(5):2427-34.

15. Silvia F, Marina Marcos V, Octavio F, Norma S, Sonia F. Comparative dissolution and polymorphism study of clopidogrel bisulfate tablets available in Argentine. J App Pharm Sci. 2020;10(10):062-72.

16. Lalitha LJ, Chenthilnathan A, Vidyasagar VJ. Process validation of clopidogrel bisulphate 75 mg tablets. Sch Res Lib. 2014;6(3):72-8.

17. Tarawneh OA, Madi AM, Hamed R, Qirem R, Qerem W, Alhusban A, et al. In vitro Characterization and Evaluation of Commercialized Paracetamol Products in Jordan. Dissolution Technol. 2019;26(1):36-44

18. Convention USP, Editor nThe Pharmacopoeia of the United States of America 1916: United States Pharmacopoeial Convention, Incorporated 2018.

19. Sidra Urooj, Rizwana I. Review article on pharmaceutical analysis of tablets according to standard pharmacopeias. J Emerg Tech & IR. 2021;8(9):474-84.

20. Barsagade P, Khetade R, Nirwan K, Agrawal T, Gotafode S, Lade U. Using RP-HPLC. Int. J of Pharma Sci Review and Res 2021;05:28-38.

21. Wojcik-Pastuszka D, Krzak J, Macikowski B, Berkowski R, Osiñski B, Musia³ W. Evaluation of the Release Kinetics of a Pharmacologically Active Substance from Model Intra-Articular Implants Replacing the Cruciate Ligaments of the Knee. Materials (Basel). 2019; 12(8): 1202.

22. Laracuente ML, Yu MH, McHugh KJ. Zero-order drug delivery: State of the art and future prospects. J Control Release. 2020;327:834-856

23. Jain A, Jain SK. In vitro release kinetics model fitting of liposomes: an insight. Chem Phys Lipids. 2016: S0009-3084(16)30147-5.

24. Drucker CT, Senger LW, Pacioles CT. Application of the weibull model to describe the kinetic behaviors of thiol decolorizers in chlorogenic acid-lysine solutions. J Food Eng. 2023;339:111287.