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Prapti J Desai
Principal, Asian college of Pharmacy, Dhayari-Narhe Rd, Tal-Haveli, Dhayari, Pune, Maharashtra, India

Priya Chidrewar
Assistant Professor, Department of pharmacy, Asian College of Pharmacy, Dhayari-Narhe Rd, Tal-Haveli, Dhayari, Pune, Maharashtra, India

Arun Sathe
Assistant Professor, Department of Pharmacy, Asian College of Pharmacy, Dhayari-Narhe Rd, Tal-Haveli, Dhayari, Pune, Maharashtra, India

Correspondence Author;
Prapti J Desai
Principal, Asian college of Pharmacy, Dhayari-Narhe Rd, Tal-Haveli, Dhayari, Pune, Maharashtra, India

Development and validation of new discriminative dissolution method for Prucalopride tablets

Prapti J Desai, Priya Chidrewar and Arun Sathe

Abstract
In order to cater to the developed market, it is necessary to have a specific dissolve process that can be used for quality control testing and product assessment in quality by design trials. The present work showcases the methodical creation of a dissolving technique that allows for discrimination of the BCS Class 2 medication Prucalopride Tablets. It is worth noting that the solubility of this medicine is significantly influenced by pH levels. Concurrently, the pH, velocity, and equipment were tuned and subjected to testing in order to assess the method's robustness, repeatability, and variability. The method's ability to discriminate was appropriately proved.

Keywords: Development, validation, discriminative dissolution method, prucalopride tablets and BCS Class 2.

1. Introduction

After the oral administration of a drug in a certain dosage form, the process of intestinal absorption of the medication may be broken down into the following sequential phases: Solubilization, dissolution, or both, and the permeability of the dissolved medication at the absorption site all play a role in the release of the active component from the drug product. The relevance of the first two steps in determining bioavailability requires the important development of an adequate *in vitro* dissolving strategy for accurate prediction of *in vivo* functioning. This is because the first two phases are responsible for establishing bioavailability. Dissolution studies are frequently useful for the following applications:

1. Determining the active pharmaceutical ingredient's (API) properties, such as particle size and crystal structure.
2. Directing the development of innovative formulations.
3. Facilitating optimum formulation selection (Ingredient selection) and manufacturing process optimization (machinery, compressive pressures, etc.) During dosage form optimization.
4. Evaluating the purity of a medicinal product from batch to batch.
5. Allowing for the comparison of samples originating from diverse manufacturing sources.
6. Comparing a brand-new or generic formulation to an existing product.
7. Determining the stability of the medication product and assisting with shelf life determination.
8. Preserving product quality when specific scale-up and post-approval modifications (SUPAC) take place, including changes to the production location, unit size, and excipient quantities.
9. Decreasing the need for bioequivalence investigations (bio waivers).
10. Laying the groundwork for constructing an *in vitro-in vivo* correlation (product performance prediction *in vivo*).

Dissolving tests are an excellent method for predicting the efficacy of medications that dissolve poorly or not at all, and for which absorption is the primary concern (i.e., pharmaceuticals in Class 2 of the Biopharmaceutics Classification System [BCS]). As an additional precaution, a melting technique with sufficient selective power is required to detect any changes in product quality before they impair the product's performance in live organisms. Dissolvability differences caused by intentional tweaks to the formulation or manufacturing process are often used to demonstrate the dissolving method's discriminating potential [1, 4]. Chronic, unexplained constipation is a common indication for Prucalopride use. It acts as a 5-HT4 receptor agonist. A medication called Prucalopride is used to stimulate digestion.

It is often used for cases of inexplicable constipation. Constipation that lasts longer than three months and can't be attributed to a medical condition is considered chronic unexplained constipation. Individuals affected by this condition may have constipation, diarrhea, or both. People who have problems urinating might benefit from taking Prucalopride. This may be helpful if you suffer from chronic or severe constipation. The agonistic medication Prucalopride has a high degree of inherent activity. It targets the 5-HT4 receptor with excellent selectivity. This improves bowel function and relieves chronic constipation because it indirectly triggers the production of acetylcholine, a chemical messenger. The gastrointestinal smooth muscle contractions are relaxed by the medication Prucalopride, which facilitates bowel movements. Constipation is relieved and normal bowel function is restored. Research [5, 6] suggests that Prucalopride may help people whose severe constipation is not relieved by laxatives.

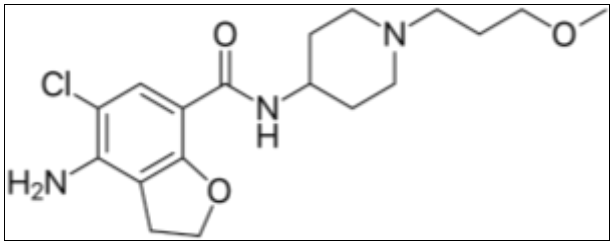

Fig 1: Chemical structure of Prucalopride

It's important to begin planning for product failure even before production is complete. Once the sample formula and process are complete, the formulator may decide how best to expand their usage. Regular quality control of industrial quantities must include evidence that the melting procedure is selective, as required by the world's leading regulatory organizations [7].

2 Materials and Methods

Each liquid used in an HPLC study was of the HPLC grade, and all other chemicals were of the analytical reagent grade and used as advised. The following chemicals were used to make buffers and the HPLC mobile phase: sodium perchlorate monohydrate (Merck, India), acetonitrile (Fisher Scientific, India), methanol (Fisher Scientific, India), sodium acetate trihydrate (Qualigens, India/Merck, India), glacial acetic acid (Fisher Scientific, India), potassium biphthalate (Merck, India), and hydrochloric acid (sd Fine chemicals, India).

2.1 Formulation Preparation

In order to manufacture film-coated tablets of Prucalopride, the following ingredients were utilized: calcium hydrogen phosphate anhydrous, Croscarmellose sodium, magnesium stearate, microcrystalline cellulose, and Opadry.

2.2 PH–Equilibrium Solubility Studies

The equilibrium solubility at different pH levels was found using the shake-flask method. 25 mL of the USP buffer solution for each pH level (1.2, 3.0, 4.5, 5.5, and 6.8) was mixed with Prucalopride to make a system with a thick sample and a liquid. After making sure the samples didn't have any extra solids, they were sonicated for 10 minutes and then put in a vibrating water bath at 37 °C. Before figuring out how much Prucalopride there was, a small sample (2 mL) was passed through a 0.45-µm PVDF membrane with an approved HPLC method. To reach balance, the solution was mixed for 24 hours [8, 10].

2.3 Dissolution Studies

Unless otherwise specified, six tablets were used in each dissolution test, which was performed at 37 degrees Celsius using the USP Apparatus 2 and a medium volume of 900 mL. Dissolution profiles were generated from samples collected at 5, 10, 15, 20, 30, 45, and 60 minute intervals. It was also decided that certain times would last 90 minutes, while others would go on forever (for example, 200 rotations per minute for 10 minutes). The samples were filtered via 0.45-micrometer polyvinylidene fluoride (PVDF) filters prior to analysis utilizing a validated high-performance liquid chromatography (HPLC) technique for the detection and quantification of Prucalopride [11, 12].

2.4 Sample Analysis

The samples were analyzed using a Waters 2695 separation module from Waters Corporation in Milford, MA, USA, coupled with a 2487 UV-vis detector. In this work, a 10 cm long, 4.6 mm in diameter Hypersil BDS C-18 column was employed for the HPLC analysis; its particles measured 3 micrometers in size. The column was maintained at a steady 25 degrees Celsius. A 55:45 solution of sodium perchlorate monohydrate (10 mM) and acetonitrile used as the mobile phase. The analyte was detected at a wavelength of 235 nm with a mobile phase flow rate of 1.5 mL/min [13, 14].

2.4.1 Estimation of Prucalopride in the dissolution samples

We used a Shimadzu liquid chromatography system (Shimadzu Corporation, Kyoto, Japan) with a model LC-10ATVP binary pump and a model SPD-M10AVP PDA detector to analyze the Prucalopride concentration in the sample solutions. The experiment used a Merck Li Chrospher® 100 RP-18 octadecyl silane column that measured 250 x 4.6 mm for the stationary phase. Column integration was done in LC Solution 1 utilizing that program. The mobile phase was a 58:32:10 mixture of methanol, acetonitrile, and a buffer solution containing 0.03M potassium dihydrogen orthophosphate (pH 4.8). Every day, the mobile phase was freshly prepared by ultra-sonicating it at low pressure to release any trapped gas. After that, a 0.45 µm-pore-size membrane filter was used to filter the produced mobile phase [5, 16]. Ten minutes were spent draining each sample at 1.2 ml/min. The injection was 20 µl in volume. At 25 degrees Celsius, the samples were tested, and detection was performed at a wavelength of 242 nm.

2.4.2 Preparation of standard stock solutions

Twenty-five milligrams of Prucalopride was mixed with

fifty milliliters of methanol to yield a stock solution with a concentration of 500 µg/ml. Using 0.1N hydrochloric acid (HCl), simulated gastric fluid (SGF), pH 4.5 acetate buffer, pH 6.8 phosphate buffer, and distilled water, seven working standard solutions were prepared with concentrations ranging from 0.5 to 10 µg/ml for this study. The solution was filtered via a membrane filter with a pore size of 0.45 µm [17] before being injected into the column.

2.5 Validation of the dissolution method

The chosen dissolving test condition was checked for sensitivity, accuracy, precision, and stability based on the most current ICH and FDA guidelines. The specificity of the dissolving medium was tested by comparing the peak interference from the dissolving medium and control to the drug using [1] a sample of the dissolving medium without the drug [2]. A way to dissolve medicine that depends on its strength the dissolving liquid also had a business tablet (product A) along with a dummy tablet. All of these samples were put through a 0.45 µm membrane filter and stirred at 100 rpm for 30 minutes before being evaluated by HPLC [18].

3. Results and Discussion

Discriminating dissolving techniques will soon be used by prominent regulatory organizations to evaluate the quality of pharmaceutical items, with a concentration on oral solid dosage forms. The following steps should be taken in advance of creating a discriminative dissolving procedure: Setting a dissolution profile goal, such as achieving an 85% dissolve rate within 30 minutes. Draw up a flowchart that details the experiments you want to do as part of your method development strategy, along with your expected outcomes and next moves. Dissolving process factors including medium, speed, equipment, and volume should be systematically optimized and settled upon. Offer proof that the results can be replicated and the technique utilized is reliable; illustrate the distinguishing features of the optimal strategy. In addition, it is suggested that you follow sink conditions, which are met when there is three times as much medicine as is required to dissolve in the dissolving solution. However, if the selective nature of the dissolving process can be convincingly shown, a departure from the sink criteria may be warranted. It is essential to have a firm grasp on the API's physicochemical characteristics before beginning the technique creation process for dissolving the API. In particular, choosing the right solvent for dissolution is facilitated by familiarity with equilibrium solubility. Prucalopride solubility is greatly affected by pH, as shown in equilibrium solubility tests, which is consistent with previous studies.

3.1 Dissolution profiles of Prucalopride tablets in different pH buffers.

At pH 1.2, solubility was 22.52 mg/mL, but at pH 3.0, it was just 1.44 mg/mL. Solubility kept dropping to a constant value of 0.12 mg/mL when pH climbed above 3.0. According to the USP, a dissolving method must contain enough time points to characterize the accelerating and plateauing stages of dissolution curves. This was deemed crucial in establishing the dissolving parameters for developing the disintegration procedure for Prucalopride tablets. The goal was to get a profile that showed an 80% drug release in 30 minutes, with some variance at each sampling site. The studies on Prucalopride solubility suggest that the medium's pH may significantly affect the drug's solubility. Dissolution of Prucalopride tablets at 50 rotations per minute in Apparatus 2 is shown in Figure 1 as a function of pH. Dissolution studies were carried out at pH 1.2, 4.5, and 6.8 to include the high, medium, and low solubility zones. Saturated solubility studies showed that, as expected, dissolution was quick and complete at low pH and sluggish and incomplete at higher pH. At a pH of 4.5, however, the dissolution curve clearly showed an upward trend and a plateau.

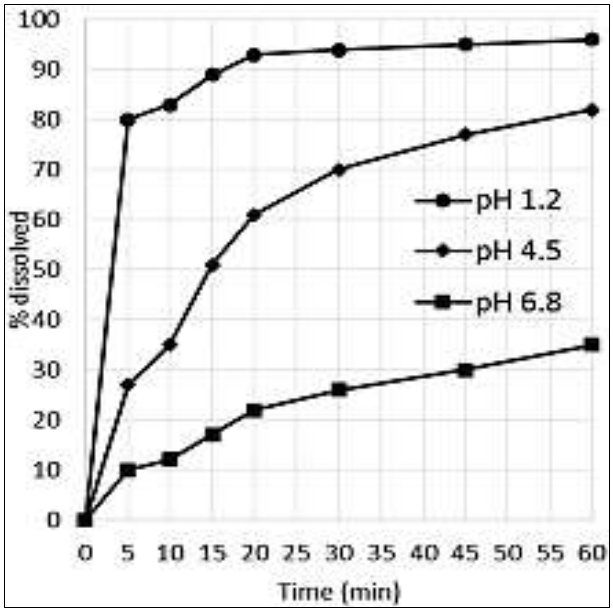

Fig 2: Prucalopride tablet dissolution profiles in distinct pH buffers. The conditions for dissolution are 900 mL, 50 rpm, Apparatus 2.

3.2 Dissolution Method of Prucalopride Tablets

The dissolving rate and depth of solubility may be improved by using surfactants. At a pH of 6.8, only partial dissolving was detected, suggesting the use of a Solubilizer would be necessary for full dissolve to occur. Prucalopride solubility was tested in three different simulated gastrointestinal fluids

(FaSSIF, FeSSIF, and FaSSIF/FeSSIF), and it was shown that adding a surfactant did not improve the drug's solubility. PH 4.5 without surfactant was used to further assess the medium's repeatability and selective properties. Unacceptable pH 4.5 fluctuation between runs was unexpectedly discovered. These factors, as indicated in Table 1, were considered throughout the process of developing a method for dissolving in order to strike a balance between pH and speed changes.

Table 1: Development Matrix for Dissolution Method of Prucalopride Tablets

pH	rpm			Comments
	50	75	100	
1.2	–	–	–	Desired discrimination not anticipated due to high solubility
2.0	–	–	–	Desired discrimination not anticipated due to high solubility
3.0	Y	FE	NA	At low rpm, discrimination was envisaged, so the remaining hydrodynamics were reserved.
4.0	Y	FE	NA	At low rpm, discrimination was envisaged, so the remaining hydrodynamics were reserved.
4.5	NA	Y	Y	Results at 50 rpm cannot be replicated.
5.0	–	–	–	Rejected due to poor solubility. Considered at pH 6.8.
6.0	–	–	–	Rejected due to poor solubility. Considered at pH 6.8.
6.8	NA	Y	Y	At low rpm, the desired discrimination is not anticipated.
Y – Experiments to be performed. FE – follow-up experiments after reviewing the results. NA – experiments not planned.				

3.3 Dissolution profiles of Prucalopride tablets

Figure 3 shows how Prucalopride pills broke down when studied with Apparatus 2 and different pH and water conditions.

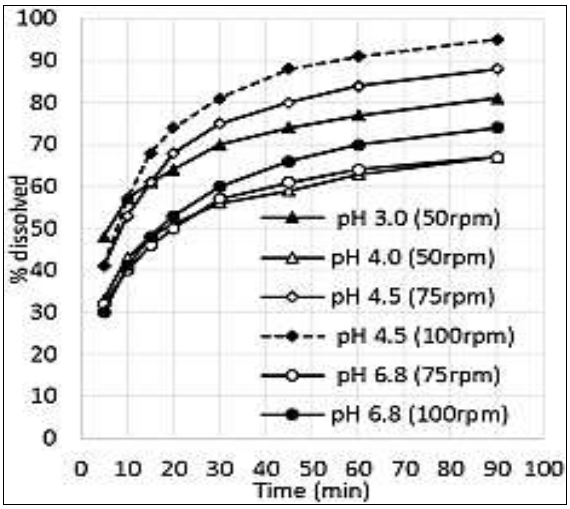

Fig 3: Dissolution profiles generated as per development matrix

At 50, 75, or 100 speed and pH 3.0, 4.0, or 6.8, the drug did not dissolve after 10 or 30 minutes. This bad dissolving was caused by either a slow dissolution rate caused by pH 6.8's non-sinking conditions or a lack of hydrodynamics to quickly mix the dissolved medicine. At 100 rpm, pH 4.5 dissolution profiles got the expected result, but at 75 rpm, dissolution was still slow (< 80% in 30 minutes). A dissolve profile was made in device 1 at pH 4.5 to help better understand how the device works at the given pH, speed, and volume.

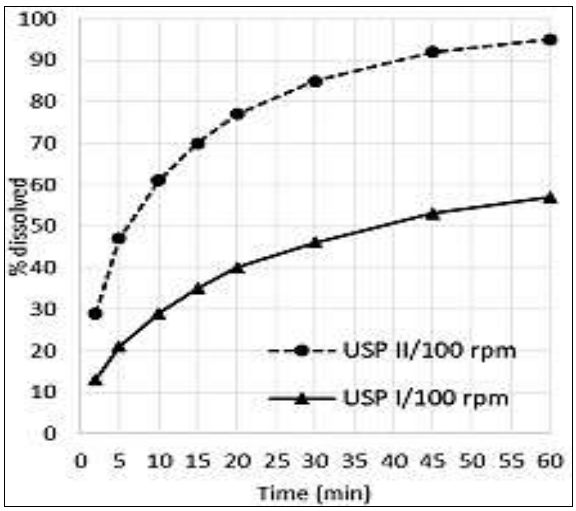

Fig 4: Effect of apparatus on dissolution of Prucalopride tablets in 900 mL of pH 4.5 acetate buffer.

Apparatus 1 at 100 rpm, as shown in Figure 4, is insufficient for processing Prucalopride tablets due to the presence of sticky residue in the basket. This led the pills to disperse unevenly, with some falling to the bottom of the container. Figure 5 displays the repeatability of the data, which led to the conclusion that dissolving the sample in 900 mL of pH 4.5 acetate buffer at 100 rpm in Apparatus 2 is the most effective method.

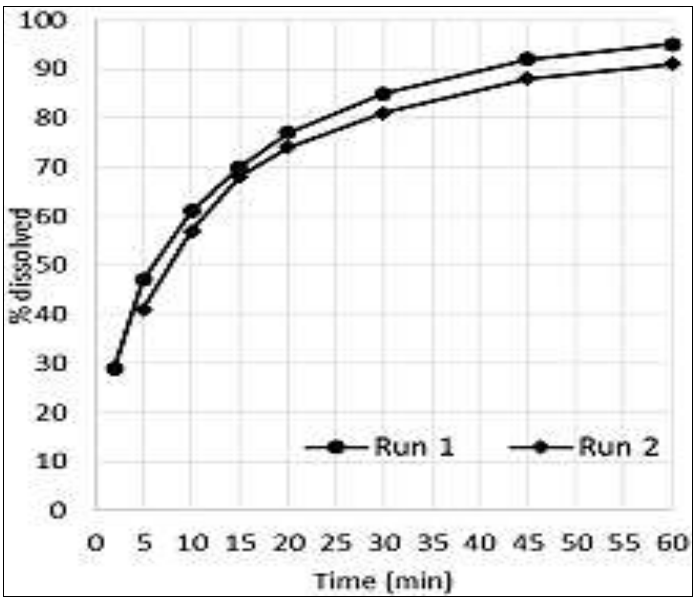

Fig 5: Dissolution profiles of the same batch of Prucalopride tablets to demonstrate run-to-run reproducibility in 900 mL of pH 4.5 buffer at 100 rpm, using Apparatus 2.

An approach is considered discriminative if it can identify substantial changes in construction and composition. Process 1 included the preparation of the combination that served as the basis for the development of the dissolving technique, using the aforementioned excipients. A formula with more calcium hydrogen phosphate anhydrous and one prepared with a different way (Process 2) were chosen to demonstrate the sensitivity of the selected dissolve process. Figure 6 depicts the final result.

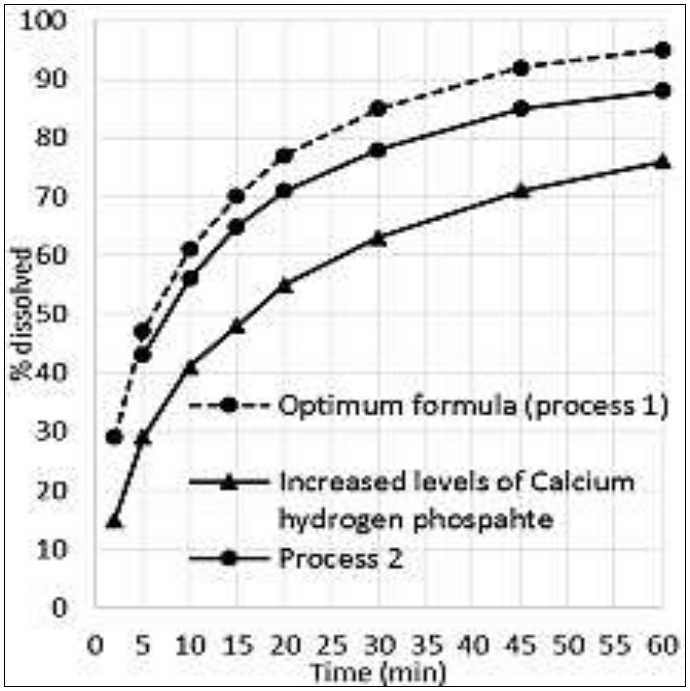

Fig 6: Dissolution profiles generated on samples with various manufacturing processes and excipient concentrations to demonstrate the discriminatory nature of the optimized dissolution technique.

The dissolution rate (f2 = 35.23) of the formula with a greater concentration of calcium hydrogen phosphate anhydrous was significantly lower than that of the baseline formula. The reason for this was the inability of dry calcium hydrogen phosphate to dissolve in liquid. The modification to the production procedure did not slow the rate of dissolution (f2 of 61.61), even if the profile was somewhat delayed. The accuracy of the selected deconstruction procedure is shown here.

3.4 PH–Equilibrium Solubility Studies

To evaluate the technique's robustness, researchers first looked at all the possible factors that may have an impact on the results during regular analysis. The research analyzed both the pH variations observed and the different quality levels of the main chemicals utilized in buffer manufacturing. The effects of adjusting the pH of the medium by ± 0.2 pH units and changing the availability of sodium acetate on the dissolving of Prucalopride tablets were investigated. Figures 7A and 7B illustrate that the typical formulation's profiles overlap heavily with those displayed. Consequently, the selected dissolution.

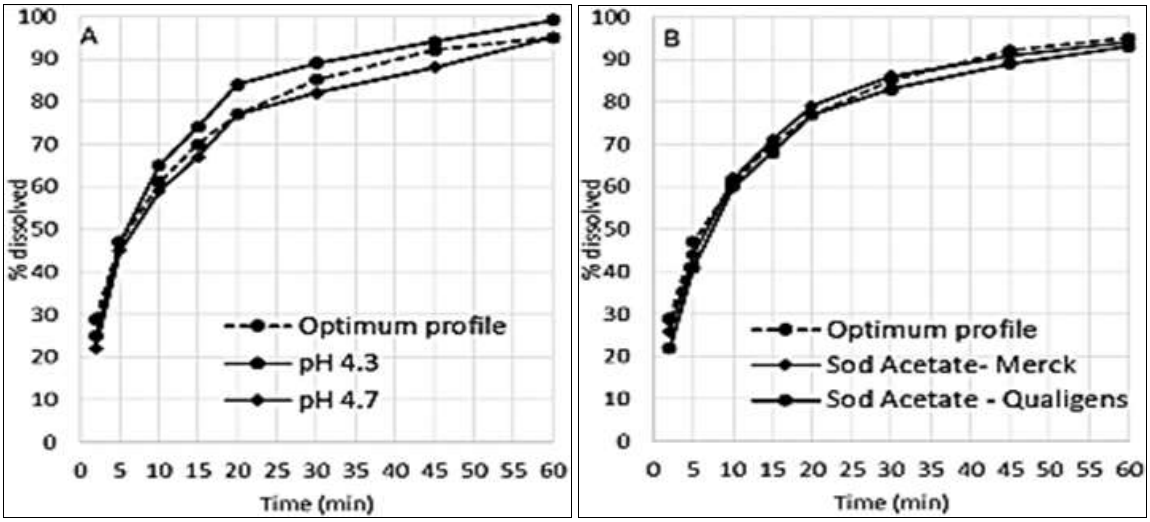

Fig 7: Effect of (A) pH and (B) grade of critical excipients in buffer preparation.

3. Validation of the dissolution method

3.5.1 Accuracy

The recovery test was carried out to evaluate the accuracy of the approach. During the accuracy test, you should aim for recoveries between 95% and 105%. Researchers showed that Prucalopride had a recovery rate ranging from 99.5% to 102.9% on average. The recovery numbers in Table 2 show that the dissolving process was successful.

Table 2: Accuracy Results for Prucalopride (% Recovery)

Sample	Concentration (%)		
	10 µg/ml	100 µg/ml	150 µg/ml
1	99.8	100.2	101.2
2	99.5	100.4	101.5
3	99.6	100.0	100.4
4	100.0	99.9	101.3
5	102.9	101.8	101.5
6	100.6	100.7	99.9
Average	100.4	100.5	101.0
R.S.D. (%)	1.28	0.68	0.64

R.S.D. indicates relative standard deviation

3.5.2 Precision

Results for the intra-day and inter-day precision are summarized in Table 3.

Table 3: Intra- and Inter-Day Precision for Prucalopride

Concentration (%)		R.S.D. (%) Intra-day	R.S.D. (%) Inter-day
Day 1	10	1.12	1.28
Day 2	10	1.47	
Day 1	100	0.74	0.68
Day 2	100	0.60	
Day 1	150	0.48	0.64
Day 2	150	0.60	

The dissolving process exhibits a high level of accuracy, as seen by the RSD value being below 2%. The evaluation of Prucalopride stability in phosphate buffer (pH 6.8) dissolving medium was conducted by assessing standards and samples. Throughout the duration of the seven-day experimental period, the drug concentration observed in the samples consistently ranged from 98% to 102% of the starting value. Furthermore, no degradation products were found in any of the chromatograms analyzed. The stability of Prucalopride was found to be unaffected by the absence of excipients and when exposed alone to the disintegration medium.

3.5.3 Percentage of drug released

Discharge percentages of medications were compared between products and across time using analysis of variance and Tukey's post hoc multiple comparison test for statistical significance. Tukey's test indicates that there is a statistically significant difference between Products A and C ($p< 0.05$), while no such difference exists between Products A and B ($p> 0.05$).

Table 4: Tukey's Multiple Comparison Test for Products

Comparison	Mean Diff	q	P	Significant $p<0.05$	95% LCL	95% UCL
A vs B	3.97	2.96	0.133	No	-1.08	9.02
A vs C	14.12	10.54	<0.001	Yes	9.06	19.17
B vs C	10.15	7.58	<0.001	Yes	5.09	15.20

Quantitative descriptions of breakdown data often include mathematical models. Fitting these models with the breakdown data allowed us to choose the one with the greatest coefficient of determination. The dynamics of drug release were analyzed using the various dissolving patterns to compare the drug release models of each product. Multiple models were applied to the Prucalopride tablet disintegration data (figure 8), including zero-order, first-order, Korsmeyer-Peppas, Hixson Crowell, Weibull, and Baker-Lon's.

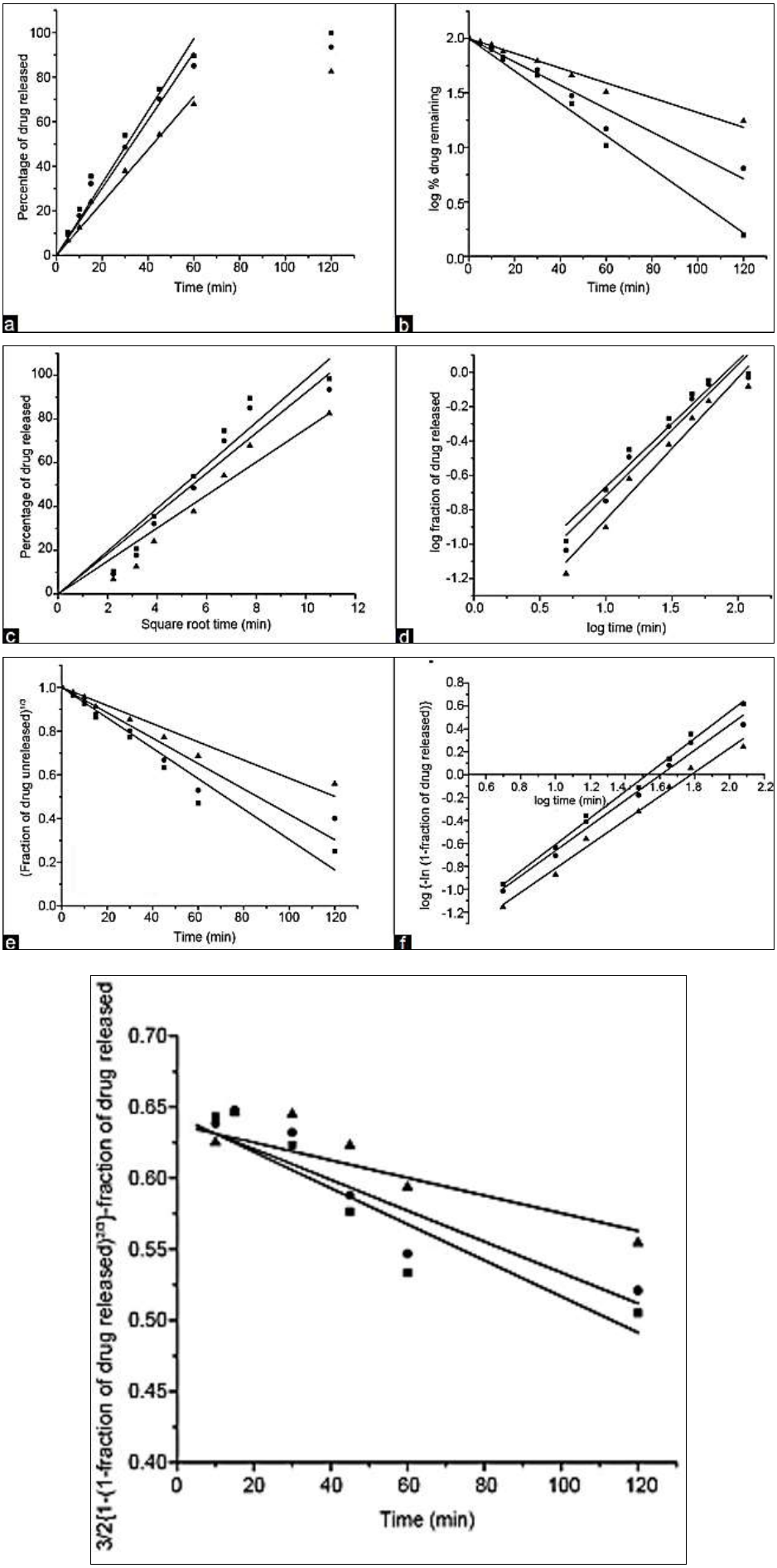

Fig 8: Model-dependent plots for products-A, B and C (a) Zero-order model (b) First-order model (c) Higuchi model (d) Korsmeyer-Peppas model (e) Hixon-Crowell (f) Weibull model (g) Baker Lonsdale model. -■- Product-A; -●- Product-B; -▲- Product-C.

4. Conclusions

The medicine under investigation was placed in BCS Class 2, and its solubility was shown to be strongly pH-dependent. The study showed how to build a selective dissolving strategy by using a methodical and sequential approach to trial design. For Prucalopride tablets, the following conditions are used in the strong and selective dissolve process: It has been discovered that using a pH 4.5 acetate buffer at a volume of 900 mL in Apparatus 2 is optimal for maintaining product quality. The current rotating speed of the system is one hundred revolutions per minute. Both the pharmaceutical industry and governmental bodies benefit from the deployment and recording of dissolving procedures for the thorough evaluation of pharmaceutical products (19). To facilitate formulation development in conformity with the most recent recommendations from the International Council for Harmonization (ICH) and the U.S. Food and Drug Administration (FDA), a novel dissolving test procedure was created and verified. Improved discriminatory skills and evidence of a statistically significant difference between Products A, B, and C were shown by the ANOVA-based technique. Weibull provides the best description of drug release from products A, B, and C, allowing for comparative evaluation of level (location) and profile shape uniformity. The acquired dissolution profiles were evaluated using the variables f1 and f2, which showed that they were comparable for Product-B but distinct from Product-C when compared to Product-A. This research demonstrates the usefulness and viability of all methods utilized to evaluate and contrast dissolution profiles. Discriminative dissolving allows for better formulation and production, as well as higher-quality and more effective tablets overall. In addition, this approach reduces the potential for releasing quantities of bio-incompatible products into the market (20-22).

5. References

1. Rossi RC, Dias CL, Donato EM, Martins LA, Bergold AM, Froehlich PE, *et al*. Development and validation of dissolution test for ritonavir soft gelatine capsules based on *in vivo* data. Int. J Pharm. 2007;338:119-24.
2. Maggio RM, Castellano PM, Kaufman TS. A new principal component analysis-based approach for testing “Similarity” of drug dissolution profiles. Eur. J Pharm Sci. 2008;34:66-77.
3. Lee SL, Raw AS, Yu L. Dissolution testing. In: Krishna R, Yu L, editors, Biopharmaceutics Application in Drug Development, New Jersey: Springer; c2008. p. 47-74.
4. Lagace M, Gravelle L, Di Maso M, McClintock S. Developing a discriminating dissolution procedure for a dual active pharmaceutical product with unique solubility characteristics. Dissol. Technol. 2004;11:13-8.
5. The United States Pharmacopoeia. The dissolution procedure: Development and validation. Pharmacopoeial Forum. 2004;30:351-63.
6. Hoti E, Censi R, Ricciutelli M, Malaj L, Barboni L, Martelli S, *et al*. Validation of an HPLC-MS method for riverine tablet dissolution analysis. J Pharm Biomed Anal. 2008;47:422-8.
7. Yuksel N, Kanik AE, Baykara T. Comparison of *in vitro* dissolution profiles by ANOVA-based, model-dependent and -independent methods. Int. J Pharm. 2000;209:57-67.
8. Brown CK, Chokshi HP, Nickerson B, Reed RA, Rohrs BR, Shah PA, *et al*. Acceptable Analytical Practices for Dissolution Testing of Poorly Soluble Compounds. Pharm Technol. 2004;28:56-65.
9. Carvalho-Silva B, Moreira-Campos LM, Nunan EA, Vianna-Soares CD, Araujo-Alves BL, Cesar IC, *et al*. Optimization and statistical evaluation of dissolution tests for Indinavir sulfate capsules. Farmaco. 2004;59:921-7.
10. He Z, Zhong D, Chen X, Liu X, Tang X, Zhao L, *et al*. Development of a dissolution medium for nimodipine tablets based on bioavailability evaluation. Eur. J Pharm Sci. 2004;21:487-91.
11. Eryol C, Demirturk E, Oner L. Preparation of meloxicam tablet formulations and evaluation of *in vitro* release similarities. FABAD J Pharm Sci. 2004;29:53-61.
12. Pokharkar VB, Mandpe LP, Padamwar MN, Ambike AA, Mahadik KR, Paradkar A, *et al*. Development, characterization and stabilization of amorphous form of a low Tg drug. Powder Technol. 2006;167:20-5.
13. Wei L, Sun P, Nie S, Pan W. Preparation and evaluation of SEDDS and SMEDDS containing Prucalopride. Drug Develop Ind. Pharm. 2005;31:785-94.
14. Agnihotri SA, Aminabhavi TM. Development of novel interpenetrating network Gellan gum-poly (vinyl alcohol) hydrogel microspheres for the controlled release of Prucalopride. Drug Develop Ind. Pharm. 2005;31:491-503.
15. Loftsson T, Vogensen SB, Desbos C, Jansook P. Prucalopride: Solubilization and cyclodextrin complexation: A technical note. AAPS Pharm Sci. Tech. 2008;9:425-30.
16. Rathod R, Prasad LP, Rani S, Nivsarkar M, Padh H. Estimation of Prucalopride in human plasma by using HPLC-fluorescence detector and its application to pharmacokinetic study. J Chromatogr B: Anal Technol. Biomed Life Sci. 2007;857:219-23.
17. FDA. Recommended Dissolution Methods, available from: [Last accessed on 2010 Jan 11]
18. Gannu R, Yamsani VV, Rao YM. New RP-HPLC method with UV detection for the determination of Prucalopride in human serum. J Liq. Chromatogr. Relat. Technol. 2007;30:1677-85.
19. O’Hara T, Dunne A, Butler J, Devane J. A review of methods used to compare dissolution profile data. Pharm Sci. Technol. Today. 1998;1:214-23.
20. Patel N, Chotai N, Patel J, Soni T, Desai J, Patel R, *et al*. Comparison of *in vitro* dissolution profiles of oxcarbazepine-HP-β-CD tablet formulations with marketed oxcarbazepine tablets. Dissol. Technol. 2008;15:28-34.
21. Costa P, Sousa Lobo JM. Modelling and comparison of dissolution profiles. Eur. J Pharm Sci. 2001;13:123-33.
22. Ahuja N, Katare OP, Singh B. Studies on dissolution enhancement and mathematical modelling of drug release of a poorly water-soluble drug using water-soluble carriers. Eur. J Pharm Biopharm. 2007;65:26-38.