Original Research Article

ASSESSMENT OF INVITRO QUALITY TESTS OF PARACETAMOL BRANDS 500mg IN KARACHI, PAKISTAN

Abstract:

Objective: The main purpose of this study is to perform the quality assessment of three different brands of Paracetamol tablets (500 mg) available in local market of Karachi, Pakistan **Methodology:** several pharmacopeial and non-pharmacopeial tests were applied on selected brands coded as P1, P2 and P3, respectively. A sample of (n = 20) tablets from each coded brand were subjected to pharmacopeial tests such as weight variation, friability, disintegration, assay and dissolution and non- pharmacopeial tests such as hardness, diameter and thickness. Dissolution data were subjected to model dependent and model independent kinetic approaches using Dissolution Data solver **Results:** The Average weight in mg, hardness in kg , thickness and diameter in mm of (n=20) tablets of brands P1, P2, and P3 were noted and their standard deviation were calculated which were found to be 520.625mg (± 0.49 mg), 519.53 mg (± 0.472 mg) and 521.20 mg (±0.494mg),7.25(±0.45kg), 7.48(±0.29kg) and 6.64(±0.11kg), 4.3(±0.15mm), 3.2(±0.15mm), 3.2(±0.11mm) and 12.2(±0.13mm), 12.4(±0.14mm) and 12.6(±0.15mm). Friability of selected brands were found to be 0.37%, 0.41% and 0.26%. Disintegration time were found to be 2minutes26seconds, 2minutes56seconds and 1minute 54 seconds. Percentage Assay of (n=20) tablets of selected brands were found to be as P1= 98.97(± 0.02%), P2= 99.96(± 0.03%) and P3= 99.91(±0.02%). Dissolution were performed at multiple point intervals such as 5 min, 10 min, 20 min, 30 min and 45 min. At 45 minutes the percentage of drug release for P1, P2 and P3 were found to be 98.7%, 99.8% and 98.9%. For the determination of model independent approaches brand P2 were selected as reference formulation. Similarity factor (*f2),* dissimilarity factor *(f1)* for brand P1, and P3 were found to be 73.5, 5 and 79.5, 3. All selected brands were subjected to model dependent approaches. In this study all tablets of selected brands P1, P2 and P3 followed First order and weibull model as the r^2 values for first order were (0.9897), (0.9893) and (0.9837) and for weibull model r^2 values were found to be (0.9937), (0.9953) and (0.9915) **Conclusion:** In this study successful application of Pharmacopeial and non Pharmacopeial tests on three different selected brands in Karachi, Pakistan were carried out however further work is recommended on large sample. Results were found to be in limit in accordance to the United States Pharmacopeia. Invitro multiple points interval dissolution studies were conducted at phosphate buffer pH 5.8 the data were subjected to several kinetic models by the application of Dissolution Data(DD solver) an add in program in Excel to determine release kinetics. Study demonstrated that all selected brands of Paracetamol 500 mg tablets followed first order kinetics and weibull model.

Key words: paracetamol, multiple point dissolution, model dependent and model independent

1. INTRODUCTION:

As oral Dosage forms are tablets, capsule, syrups and suspension among them tablets are widely available dosage form as they are easy to prepare, provide dose accuracy and cost effective. The foremost duty of all Pharmaceutical manufacturers is to produce products that meet all the formulation standards as specified in official standard books that not only increases patient compliance in terms of acceptance but also reduces drug toxicity related morbidities and mortalities (Iqubal et al., 2014). As the dosage form comprises of active pharmaceutical ingredient (API) and excipients. In tablets excipients serve to provide required weight and hardness , also serve to control the release rate of Active ingredient from drug(Ngwuluka et al., 2010). In syrup and suspension excipient serve to control viscosity, mask the bitter taste of drug and help in maintaining the suspended particles remain in contact with the vehicle. There are number of available products of same chemical entity(generic product) with different brand names must complies the standard of quality, safety and efficacy as the innovative product in order to ensure batch to batch uniformity as the factors can influence the total drug release from the dosage form which ultimately affect the absorption and elimination of drug (Chandrasekaran et al., 2011). It is the duty of Drug Regulatory Authority of Pakistan (DRAP) to evaluate the quality products (Binega et al., 2013). According to WHO (world Health organization) it is the duty of manufacturers to continuously evaluate the quality of products they are manufacturing (Organization, 2007).There is a need of continuous post marketing surveillance for all therapeutic agents as there are number of counterfeit and substandard drugs available in the market which can lead to therapeutic loss, loss of public confidence and increase number of side effects (Sulieman et al., 2017). As paracetamol is the most frequently used anti-pyretic (fever reducer) and pain killer in cold and flu. The chemical name of paracetamol is N- acetyl –P aminophenol can be administered by several routes such as oral, rectal and intravenous route. The molecule of this drug was first introduced in 1893 but due to the production of methaemoglobenemiea the use of this drug was avoided for 60 years (Bertolini et al., 2006) then after a prolonged research Paracetamol was first introduced as an oral formulation in USA in 1950 (Krenzelok and Royal, 2012). Paracetamol belongs to BCS Class I drug because of its High solubility and permeability(Rathnayake et al., 2016). Paracetamol reduces pain by inhibition of prostaglandin synthesis by inhibiting central Cyclooxygenase (COX-1, COX-2 and COX-3) enzymes (Smith, 2009). Paracetamol can be used by the patient of peptic ulcer safely because the molecules of this drug has no damage effect on GIT layer(Bertolini et al., 2006).over dose of this drug can lead to fetal hepatotoxicity (Vermeulen et al., 1992).The aim of this study is to evaluate the Invitro quality parameters of 3 different available brands of Paracetamol 500mg in Karachi Pakistan with the standards set by USP and BP. Invitro Dissolution studies carried out at multiple point intervals. In this study release data were fitted to several kinetic models such as model dependent and model independent approaches to evaluate the release behavior of Drug. The main objective of the study was to perform Pharmacopeial and non pharmacopeial tests on three different selected brands of Paracetamol 500 mg in Karachi, Pakistan. In this study Dissolution test were conducted at multiple point intervals which were subjected to several kinetic models such as model independent and model dependent approaches to determine the release behavior of selected drug.

MATERIALS:

Randomly three different brands of paracetamol were selected from local market of Karachi, Pakistan and coded as P1, P2 & P3 for ethical concerns identification of manufacturer is blinded and only researcher know the actual manufacturer and their Invitro quality evaluation test were carried out such as weight variation, hardness, thickness, Diameter, Assay and Invitro dissolution test.

1.1. Softwares used

Microsoft excel^{TM}2010 and Dissolution Data (DD solver) an add-in program were used for the analysis of drug release data.

1.2. Equipments and chemicals

Analytical balance (Shimadzu, Japan), Vernier Caliper (Seiko, China), digital hardness tester, Friability Tester (Curio FB 2020, Pakistan), USP Basket-rack assembly (DA 6D, Veego, India), UV spectrophotometer (Shimadzu, Japan) and USP dissolution apparatus type II (Curio, Pakistan).

Sodium Hydroxide and Potassium dihydrogen orthophosphate.

2. METHODS:

Pharmacopeial Tests:

2.1. Weight Variation Test

Twenty tablets were taken from each selected brand P1, P2, and P3. Tablets were placed individually on analytical balance. Weight of individual tablets were noted. Results were evaluated using Microsoft excel^{TM}2010. The mean weight and standard deviation were also calculated (Alsaifi and Alyahawi, 2018).According to USP the percentage difference from average weight ± 5%. Not more than two tablets of individual weight should deviate from the average weight otherwise repeat the above procedure.

Chart 1 : VARIATION LIMITS ACCORDING TO USP:

Mean Weight of Tablet	*% Difference*
Less than 130 mg	**± 10**
Greater than 130 and 324mg	**± 7.5**
Greater than 324 mg	**± 5**

2.1.1. Friability Test

Twenty tablets were selected from each selected brand individually and their initial weight were noted then placed these tablets in plastic chamber of Roche friabilitor which rotates at 25 rpm for 4 minutes after complete rotation and tablets were weighed again and their final weight noted. Friability was calculated by using formula (Kalakuntla et al., 2010).

Friability= initial weight- final weight/ initial weight * 100

Repeat the same procedure for all tablets coded P2 and P3.

Acceptance Limits:

According to USP, for conventional tablets, % friability should be < 0.5 to 1 %

2.1.2. Disintegration Test

Select 12 tablets from each coded brands and test their disintegration. The test was conducted in water at 37 ± 2 °C (Gupta and Gupta, 2016) in disintegrator. Place tablet individually in each tube (6) of the both basket assembly from coded brand P1 and repeat the same test for coded brand P2 and P3. Note the time when the tablet completely disintegrated and no single fragment remain on the mesh.

Acceptance Limits:

According to the USP the maximum disintegration time should not more than 15 minutes.

2.1.3. Assay

Weigh 20 tablets individually and note their average weight now crush the tablets in mortar and pestle. Weigh powder equivalent to 0.15 gm of paracetamol and place in 200 ml volumetric flask then add 50 ml of 0.1 M NaoH in volumetric flask now add 100 ml

of distilled water and shake it well for 15 minutes then add sufficient distilled water to produce 200 ml to make up the volume up to the mark then filter the solution. Take 10 ml of prepared solution and place in 100 ml of volumetric flask then add 10 ml of NaoH and make up the volume to 100 ml with Distilled water. Take absorbance of sample and standard at 257nm in UV spectrophotometer and calculate % Assay. If one or more tablets donot meet the Acceptance limit then repeat the same procedure for 20 tablets at that time none of the tablet should fall outside the acceptable criteria range.

Acceptance Limits:

According to USP monograph not less than 90% and not more than 110.0 % (USP35-NF30, 2016)

2.1.4. Dissolution Test

Dissolution test were performed in USP type II apparatus Paddle method at 37 $\pm$ 2 °C at 50 rpm using 900 ml of Phosphate Buffer pH 5.8. Sample of 10 ml were withdrawn at multiple time intervals such as 10, 20, 30 and 45 minutes and place it in 200 ml volumetric flask and same volume were replaced by the fresh phosphate buffer medium Samples were diluted with 0.1 M NaoH and make up the volume up to the mark. Absorbance of the sample measure at wavelength of 257nm in UV spectrophotometer against standard solution using 0.1 M NaoH as blank.

Acceptance Limits:

According to USP not less than 80 % in 30 minutes (USP35-NF30, 2016).

2.1.4.1. Analysis of Release kinetics

In vitro Dissolution testing data were fitted to various kinetic model such as model dependent (First order, Higuchi, Hixon Crowell, Weibull model) and model independent method (difference factor *(f1)* and similarity factor *(f2)*) using following formulas:

2.1.4.2. Model Dependent Approaches

Q_0 and Q_t represent the initial amount of drug in dosage form and amount release at time t

$$\mathbf{Log\ Q = LogQ_0 - \frac{kt}{2.303}} \quad \textbf{(1)}$$

Here K is the First Order Rate constant and t= time (Bourne et al., 2002)

$$\mathbf{Q = kt^{\frac{1}{2}}} \quad \textbf{(2)}$$

K=constant, t= time therefore the rate of drug release is proportional to the square root of time (Higuchi, 1963)

Higuchi constant is represented by K_{HZ}

$$\mathbf{Q_0^{1/3} - Q_t^{1/3} = K_{HC} \times t} \quad \textbf{(3)}$$

K_{HC} is Hixson–Crowell Rate constant

Q_t = Amount of drug release in time Q_0 = the initial amount of drug, k_{HC} = rate constant and t= time (Hixson and Crowell, 1931)

Weibull model described for different dissolution mechanisms. In this equation, M is the amount of drug dissolved as a function of time t. M_0 is total amount of drug being released. T accounts for the lag time. This model is useful in comparing the release patterns of matrix system

$$\mathbf{m = 1 - exp\left[-\frac{(t-Ti)^{\beta}}{\alpha}\right]} \quad \textbf{(4)}$$

Eq.4 is arranged as follows:

$$\mathbf{Log[-ln(1-m)] = b\ log(t-Ti) - log\alpha} \quad \textbf{(5)}$$

It describes the accumulated amount of drug "m" in solution at time t (Paarakh et al., 2018)

2.1.4.3. Model independent

Difference factor (*f1)* and Similarity factor of (*f2)* of dissolution data will be accessed by following equations

$$\mathbf{f_1 = \left[\frac{\sum_{t=1}^{n}(R_t - T_t)}{\sum_{t=1}^{n} R_t}\right] \times 100} \quad \textbf{(6)}$$

$$\mathbf{f_2 = 50 \times log\left\{\left[1 + \left(\frac{1}{N}\right)\sum(Ri - Ti)^2\right]^{-0.5}\right\} \times 100} \quad \textbf{(7)}$$

Number of samples (n), % release of the reference (Rt) and test (Tt) products.

Acceptable limits

The values of dissimilarity factor (*f1*) lies between 0-15 and similarity factor (*f2*) limits are in the range of 50-100.

Non- Pharmacopeial Tests:

2.1.5. Hardness Test

Twenty tablets from each selected brand were individually place in digital hardness tester Results were analyzed using Microsoft excel^{TM}2010. The mean Hardness and standard deviation were also calculated (Chandrasekaran et al., 2011)

Acceptance Limits:

The preferable hardness should be in between 6 to 12.5 kg (USP35-NF30, 2016).

2.1.6. Thickness and Diameter variation

Thickness and Diameter of 20 tablets from each selected coded brands were measure through varnier caliper by placing the tablets in the lower jaws of Vernier caliper although these are not pharmacopeial test but necessary to evaluate the quality of tablets packing. Results were analyzed using Microsoft excel^{TM}2010. There mean thickness and Diameter with standard deviations were also calculated.

Acceptance Limits:

Average diameter and thickness of 20 tablets should be in ± 5 % range (USP35-NF30, 2016).

4. RESULTS

Paracetamol is widely administered over the counter analgesic and antipyretic agent. Although several brands of Paracetamol are available in Karachi, Pakistan. In this study only three brands were selected for the assessment of in vitro quality test due to researchers own limitations. Different Pharmacopeial and non pharmacopeial test were carried out in which Pharmacopeial tests included weight variation, friability, disintegration, Assay and dissolution. The acceptance limit of all in-vitro test were according to the USP (United States Pharmacopeia). The Average weight of twenty tablets from each coded brand were noted and their standard deviation were calculated. For brand P1 it was found to be 520.62(± 0.490mg), P2= 519.53 (± 0.472mg) and P3= 521.20 (± 0.494 mg). The percentage friability of brand P1, P2 & P3 tablets were found to be 0.37%, 0.41% and 0.26%. Disintegration time of tablets of P1, P2 & P3 were found to be as 2minutes 26 seconds, 2 minutes 56 seconds and 1 minute 54 seconds as shown in **Table 1.** In this study the mean percentage Assay and standard deviation of n= (20) tablets from each selected brands P1, P2 & P3 were found to be as 98.97(± 0.02%), 99.96(± 0.03%) and 99.91(± 0.02%) as shown in **Table 2**. **Figure: 1** In this study multiple point Dissolution of paracetamol 500 mg tablets were performed by using 900 ml of Phosphate buffer pH 5.8 in USP type II Paddle apparatus at 50 rpm. 10 ml of samples with drawl at 5min, 10 min, 20min, 30 min and 45 min. At 45 minutes the percentage of drug release for coded brans P1, P2 and P3 were found to be 98.7%, 99.8% and 98.9% as shown in **Table 3. Figure 2:** Invitro dissolution data of selected brand tablets were subjected to model independent approaches. P2 brand were selected as reference tablet to determine similarity factor *(f2)* and dissimilarity factor *(f1)* because of small difference in assay and dissolution compared to P1 and P3 although all three coded brands were in limits according to United States Pharmacopeia. Similarity factor *(f2)* for P1 formulation were found to be 73.5 and dissimilarity factor *(f1)* were found to be 5 as shown in **Table 4.** For coded tablets P3 Similarity factor *(f2)* were 79.5 and dissimilarity factor *(f1)* were found to be 3 as shown in **Table 5**.In this study model dependent approaches determine the release kinetics of

drug the r^2 value of all tablets coded P1, P2 and P3 for first order kinetics were found to be (0.9897), (0.9893) and (0.9837) whereas r^2 value for Higuchi model were found to be (0.9679),(0.9226) and (0.9627). The r^2 value for Hixon Crowell model were found to be (0.9504), (0.9414) and (0.9394) and the r2 for weibull model were found to be (0.9937), (0.9953) and (0.9915) as shown in **Table 6**. Non Pharmacopeial tests included hardness, diameter and thickness. In this study hardness tablets from each coded brand were determined using Digital hardness tester. The average hardness of twenty tablets from each coded brand were noted and their standard deviation were calculated which were found to be as P1= 7.25 (± 0.45kg), P2= 7.48 (± 0.29 kg) and P3= 6.64 (± 0.11kg) as shown in **Table 1.** The average thickness and standard deviation of tablets coded P1, P2&P3 were found to be 4.3 (± 0.15mm), 3.2 (± 0.15 mm) and 3.2 (± 0.11mm). Whereas average diameter were found to be 12. (± 0.13mm) , 12.4 (± 0.14mm) and 12.6 (± 0.15mm) as shown in **Table 1**.

5. Discussion

Many factors can affect tablet weight such as compression force, speed of machine, flow properties of powder, granules density and non-uniformity of particles can lead to weight variation in tablets(Farhana et al., 2018). Weight variation serves as an important indicator of amount of Active Pharmaceutical ingredient in the formulation as well as good manufacturing process GMP followed by the manufacturer and also contribute to proper hardness and friability(Seitz and Flessland, 1965)**.** This study showed that the average weight of all selected tablets brands P1, P2 and P3 were in limits in accordance to United States pharmacopeia with ±5% deviation. For all tablets friability is the major tool to evaluate the ability of tablets to withstand pressure during shipping According to USP limit of friability should be less than 1%. Friability test ensure that all tablets are mechanically stable (Kalakuntla et al., 2010) in this study all tablets % friability of selected brands P1,P2 and P3 was less than 1%. Disintegration test showed how much time tablet is required to break in to granules which is the first step towards Dissolution process. Pharmacopeia specifies that disintegration time for uncoated tablet should be not more than 15 minutes(Qureshi et al., 2016) carried out disintegration test on five different brands of paracetamol available in Karachi, Pakistan. Disintegration is one of the most important Invitro quality test to determine batch to batch consistency and it ensure reproducible bioavailability(Tarawneh et al., 2019). As excipients has a great impact on the disintegration time because the superdisintegrants can disintegrate tablets within seconds. In this study n= (12) tablets from each brands P1,P2 and P3 were subjected to disintegration tester in distilled water at temperature 37 ± 0.5°C all tablets disintegration time were found to be less than 15 minutes. Assay test determines the amount of active Pharmaceutical ingredient API in the sample. According to the United States Pharmacopeia monograph the limit of Paracetamol Assay is not less than 90% and not more than 110.0 %. Assay test were performed for 7 different brands of paracetamol in Bangladesh which were in limits as specified in Pharmacopeia (Farhana et al., 2018). In this study all selected Paracetamol500 mg tablets brands P1,P2 and P3 Assay were found to be greater than 90%. As dissolution process is one of the most important invitro quality evaluation test that reflects the absorption and Bioavailability of Drug(Pabla et al., 2009). Dissolution studies of Seven different brands of Paracetamol in Bangladesh were performed at phosphate buffer pH 7.4 (Rahman et al., 2021). In this study multiple point Dissolution of

paracetamol 500 mg tablets were performed by using 900 ml of Phosphate buffer pH 5.8 in dissolution United States Pharmacopeia type II Paddle apparatus at 50 rpm. 10 ml of samples with drawl at 5min, 10 min, 20min, 30 min and 45 min. In this study at 30 minutes drug release were greater than 80% which was under the limit as specified in Unites states Pharmacopeia not less than 80% in 30 minutes. Dissolution data were subjected to model independent approaches that can be determined in to pair wise procedure like similarity factor (*f2)* and dissimilarity factor *(f1)*(Usta et al., 2018). Dissolution data of Flurbiprofen were subjected to several kinetic models such as model independent and model dependent approaches. The limits of dissimilarity factor (*f1*) were 0-15 and for similarity factor *(f2)* limits were 50-100 the values were calculated by using equation 6 and 7. In this study (*f1*) and (*f2*) for P1 and P3 brand were found to be in the specified limit. model dependent approaches such as First order, Higuchi model, Hixon Crowell model and weibull model were calculated through equations *eq 1,2,3,4 and 5* by using Dissolution Data solver an add in program in Microsoft ^{TM} excel 2010. Scientist used different mathematical models to estimate the release kinetics of test and reference product. (Zhang et al., 2010). In this study on the basis of r^2 value of all tablets coded P1, P2 and P3 closes to 1 followed first order kinetics (0.9897), (0.9893) and (0.9837) and weibull model (0.9897), (0.9893) and (0.9837). There is a great impact of Hardness on the disintegration of tablets. Hardness is one the important physical parameter to measure the ability of the tablet to with stand pressure during handling, packing and during shipping (Banker and Anderson, 1991). Hardness of five different brands were carried out in Bangladesh (Karmakar and Kibria, 2012).According to the united states Pharmacopeia the limit of paracetamol 500 mg hardness is 6-12 kg (USP35-NF30, 2016). Tablet problems such as weight and content of uniformity can be estimated at the early step by the determination of thickness and diameter. (Qureshi et al., 2016) determine the diameter and thickness of 5 different brands of paracetamol. In this study twenty tablets were taken from each coded brands and their thickness and diameter were noted with the help of Vernier caliper and their standard deviation were calculated which were found to be in limit with ± 5% deviation.

6. Conclusion

In this study Invitro quality tests which included pharmacopeial tests (weight variation, Friability, Disintegration, Assay and Dissolution) with non pharmacopeial tests (Hardness, Diameter and thickness) were carried out on three different brands of Paracetamol 500 mg available in Karachi, Pakistan .Although this study is based on limited brands available in the market and there is a need of large sample size. Such type of studies help manufacturers to enhance the quality of product and maximize patient compliance Multiple Point dissolution studies were carried out which were subjected to several kinetic models such as model dependent and model independent approaches by the successful application of Dissolution Data (DD Solver) an add-in program in Micro soft excel™. This study reveals that all tablets of Paracetamol followed first order and weibull model.

Table 1: PHARMACOPEIAL AND NON- PHARMACOPEIAL TEST OF PARACETAMOL TABLETS 500mg.

s.no	Formulation code	Weight (mg) Mean ±SD(n=20)	Hardness(kg) Mean ±SD(n=20)	Thickness(mm) Mean ±SD(n=20)	Diameter (mm) Mean ±SD(n=20)	Friability (%) (n=20)	Disintegration n=(6) not> 15 (minutes)
1	P1	520.62±0.490	7.25±0.45	4.3±0.15	12.2±0.13	0.37%	2minutes26sec
2	P2	519.53 ± 0.472	7.48±0.29	3.2±0.15	12.4±0.14	0.41%	2minutes56sec
3	P3	521.20±0.494	6.64±0.11	3.2±0.11	12.6±0.15	0.26%	1minute 54 sec

* SD= Standard Deviation

TABLE 2: ASSAY TEST OF PARACETAMOL TABLETS 500mg.

% strength (n=20)			
No. of Tablets	**P1**	**P2**	**P3**
20	98.95	99.92	99.98
20	98.98	99.97	99.91
20	98.99	99.99	99.94
MEAN	98.97	99.96	99.91
SD	0.02	0.03	0.02

Fig: 1 Percentage Assay of selected Brands of Paracetamol 500 mg

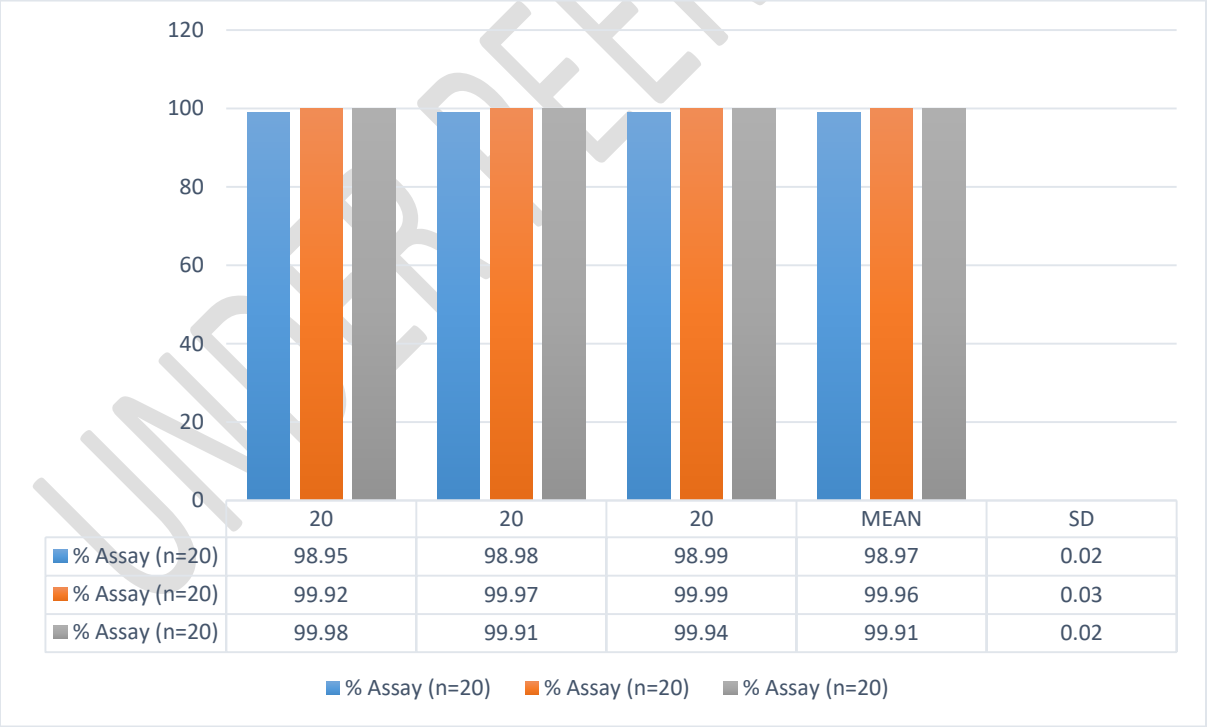

TABLE 3: MULTIPLE POINT DISSOLUTION STUDIES OF PARACETAMOL 500 mg

Time minutes	% Drug dissolved in 45 mins at λmax= 257 nm Phosphate Buffer pH 5.8		
	P1	P2	P3
5	33.4	37.8	36.7
10	53.4	58.7	54.3
20	75.5	79.8	75.1
30	85.6	89.6	88.6
45	98.7	99.8	98.9

Fig 2: Percentage of Drug Dissolved in 45 minutes at Phosphate Buffer pH 5.8

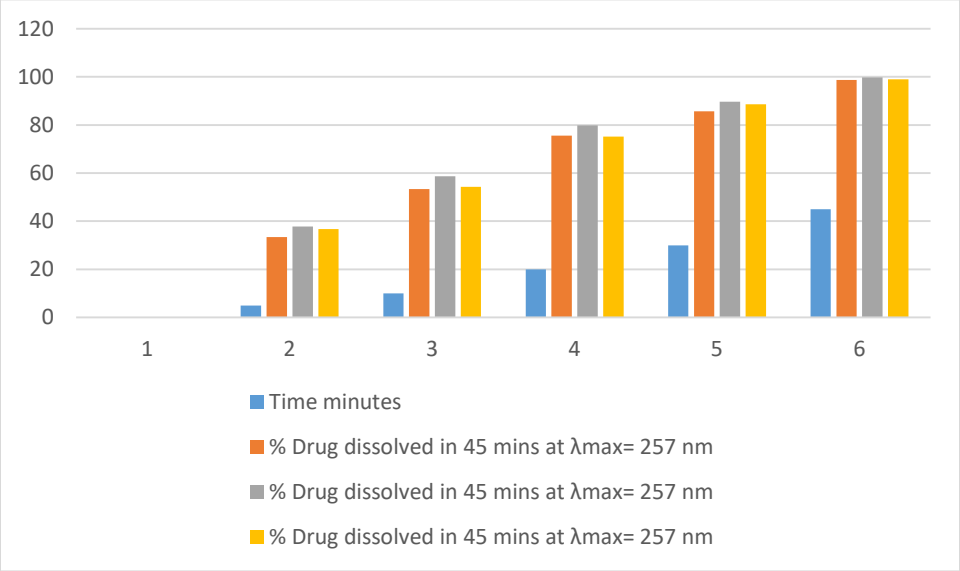

TABLE 4: f_1 AND f_2 TESTS FOR P1 WITH REFERENCE FORMULATION (P2)

Time	Rt	Tt	{Rt-Tt}	$(Rt-Tt)^2$
5	37.8	33.4	4.4	19.36
10	58.7	53.4	5.3	28.09
20	79.8	75.5	4.3	18.49
30	89.6	85.6	4	16
45	99.8	98.7	1.1	1.21
		sum (Rt-Tt)		19.1
		sum $(Rt-Tt)^2$		83.15
		sum Rt		365.7
		Similarity factor f2		73.58333
		Difference factor f1		5

Table 5: f_1 AND f_2 TESTS FOR P3 WITH REFERENCE FORMULATION (P2)

Time	Rt	Tt	{Rt-Tt}	$(Rt-Tt)^2$
5	37.8	36.7	1.1	1.21
10	58.7	54.3	4.4	19.36
20	79.8	75.1	4.7	22.09
30	89.6	88.6	1	1
45	99.8	98.9	0.9	0.81
		sum (Rt-Tt)		12.1
		sum $(Rt-Tt)^2$		44.47
		sum Rt		365.7
		Similarity factor f2		79.57947
		Difference factor f1		3

Table 6: RELEASE KINETICS OF CODED TABLETS OF PARACETAMOL 500 mg

Coded Tablets	First Order		Higuchi		Hixon Crowell		Weibull Model		
	r^2	k_1(m)	r^2	$k_H(m^{-1/2})$	r^2	$k_{HC}(m^{-1/3})$	r^2	B	α
P1	0.9897	0.074	0.9679	15.565	0.9504	0.020	0.9937	0.920	10.983
P2	0.9893	0.0086	0.9226	16.250	0.9414	0.023	0.9953	0.902	9.070
P3	0.9837	0.077	0.9627	15.804	0.9394	0.021	0.9915	0.892	9.733

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