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COMPARATIVE PHARMACEUTICAL QUALITY CONTROL TESTING OF DIFFERENT BRANDS OF PARACETAMOL TABLETS AVAILABLE IN THE TRINIDAD & TOBAGO, WEST INDIES

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ABSTRACT: Paracetamol tablets are popular over the counter (OTC) products among the patients as a good analgesics and antipyretics. The objective of this study was to compare the quality of the paracetamol tablet formulations those are locally available in Trinidad & Tobago pharmaceutical market manufactured by various pharmaceutical companies with pharmacopoeia standards. The four popular brands (A, B, C, D) of paracetamol conventional tablet of 500 mg strength were chosen. The paracetamol tablets were obtained from government hospital pharmacies as well as from local private pharmacies. To compare the quality of tablet formulations of different brands various official parameters like friability, weight variation, disintegration time, dissolution and drug assay tests were performed as per the pharmacopoeia. The result of all these parameters of different brands were in the pharmacopoeial limits so it could be concluded that marketed pharmaceutical tablets of paracetamol of these brands are safe, effective and efficacious as well as satisfy quality control limits of pharmacopoeia.

INTRODUCTION: Pracetamol or acetaminophen is a non-steroidal anti-inflammatory drug (NSAID) available as OTC commonly used as analgesic and antipyretic in the management fever and as well provide relief from mild to moderate pain. Paracetamol (acetaminophen) has weak anti-inflammatory effects since it has poor ability to inhibit cyclooxygenase (COX) in the presence of high concentration of peroxides, as are found at sites of inflammation. Chemically paracetamol is 4-hydroxy acetanilide

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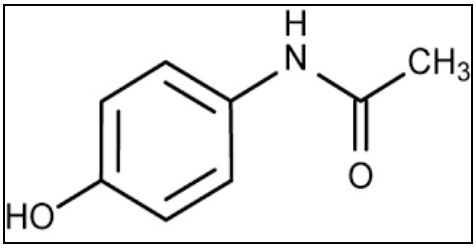

FIG 1: PARACETAMOL CHEMICAL STRUCTURE

The safety, effectiveness and efficacy of pharmaceutical dosage form can be guaranteed when its quality is reliable and to confirm the quality of pharmaceutical dosage form it is required to perform the evaluation tests as per the official books like USP, BP, IP etc.[1-5]

For the conventional tablets weight variation, friability, disintegration, dissolution, drug assay,

uniformity of contents are the evaluation test those are required to perform to confirm about the quality of tablet.

Friability is the tested for a tablet to see whether the tablet is stable to abrasion or not, it is tested by using Roche friabilator and 1% maximum loss in the weight after friability test is allowed.

Weight variation test is performed to check that the manufactured tablets have a uniform weight. As per USP following limit for the tablets (**Table 1**)

TABLE 1: WEIGHT VARIATION TEST LIMIT AS PER USP

Average weight (mg)	Maximum percentage difference allowed
130 or less	±10
130-324	±7.5
More than 324	±5

Disintegration test is performed to see how much time a tablet takes to break down in to the small particles as this is first step before the drug dissolution in the body. The condition of this test should be same like in the body as this is the part of *In-vivo-In-vitro* correlation.

The dissolution test provide the information about the drug release pattern and it is close proximate to bioavailability so it gives the information about the safety and efficacy of the dosage form. The drug assay study provide the information how much practically available in the given dosage form and after comparing with the theoretical value, a result about the efficacy can be given.[6-9]

MATERIALS AND METHODS:

Four different brands of Paracetamol tablets were obtained from the Pharmacy of Eric Williams Medical Science Hospital, Mount hope and some from the local private pharmacies. The paracetamol pure drug powder purchased from the Sigma eldritch and other solvents purchased from the local market of AR grade.

For weighing ADAM AFA-120 LC balance was used. To measure the pH of solutions OAKTON pH meter was used, Maxi Mix –II was used for mixing purpose, Electrolab EF-2 was used for friability testing, Electolab ED-2L was used for disintegration process, Electolab EDT- 08Lx was used for the dissolution study and for UV-Visible spectrophotometer analysis Agilent 8453 instrument was used.

The different brands of paracetamol tablets those are available in the Trinidad local market were given their code A, B, C, D.

Weight variation test: The purpose of this test is to verify the uniformity of each batch which ultimately reflect the drug content uniformity in all the formulation batches. The test was performed as per the official procedure, 20 tablets were randomly selected and weighed individually and also average was calculated. The difference between average and individual was calculated, further % weight variation was calculated and compare with the USP limits.[5, 7]

Friability test [7-9]: This test is usually performed to check possible wear and tear loss in the tablet during the transportation and this is closely related to tablet hardness. It is usually performed in the Roche Friabilator. Randomly 10 tablets were selected and their initial weight (W1) was recorded and after that these weighed 10 tablets were placed in the friabilator and the friabilator was operated for four minutes at 25 rpm speed and 100 revolutions, the tablets were weighed again (W2) and the percent loss (Friability) was then calculated by using following formula

$$\% \text{ Friability} = \frac{(W1 - W2)}{W2} * 100$$

The official permissible limit for friability is 1%.

Disintegration test: Disintegration is the process of breaking the tablet in to the small granules and it is prior step of drug dissolution so it is the part of *In-vitro- In vivo* correlation so the disintegration test determine the time required to breaking the tablet and pass all the particle from mesh size 10. USP disintegration apparatus (Electolab ED-2L) containing six glass tubes was used for the purpose. The disintegration test was performed as USP and to determine the disintegration time, one tablet of paracetamol was placed in each tube and the basket rack is positioned in a 1L beaker containing

distilled at 37±2°C temperature. The instrument was operated with a motor driven device with 28-32 cycle/min frequency. When all the particles from all the six tubes passed from the tube mesh to the outer beaker that time was noted as disintegration time after that the average time was noted and this process was repeated for all four different brands of paracetamol tablets. For the uncoated tablet the disintegration time limit is 15 minutes. [10, 11]

Dissolution test: Dissolution test is close proximate to the bioavailability this is the reason it is required to perform to confirm drug release pattern of the dosage form as well as efficacy of dosage form. This test is the part of *In-vitro-In-vivo* correlation so all the parameters of this test was set as per the *In-vivo* condition of human body. The dissolution test was performed by using Dissolution Tester-USP (Electrolab EDT- 08Lx) of type 2. To determine drug release 900 ml of phosphate buffer, pH 5.4 was used as dissolution medium. The 5, 10, 15, 30, 45, 60 minutes were set as a sampling time. The dissolution medium was heated up to 37±0.5°C by an auto heater. One tablet was put into all six baskets and stirred immediately at 50 revolutions per minute (rpm). After specified time intervals the 5 ml solution was withdrawn, diluted it with fresh solvent and the amount of dissolved Paracetamol was determined from UV-Visible spectrophotomter (Agilant 8453)by taking absorbance at the wavelength of maximum absorbance at about 243 nm in comparison with a standard Paracetamol solution in the same medium (Phosphate buffer pH 5.8). By measuring the absorbance, the percentage (%) of drug release was calculated. [9, 11, 12]

Drug Assay:

This is required to confirm that the labelled amount of drug is available in the given dosage form. To perform this test twenty paracetamol tablets were selected randomly and crushed them in the mortar and powder was made. The equivalent powder containing about 0.15 g drug was taken in the beaker and dissolved in 100 mL of water. The mixture was made uniform by the help of Maxi Mix-II instrument. About 0.1 mL solution was taken, diluted it upto 10 mL and absorbance at the wavelength of maximum absorbance at about 243 nm by measured by the help of UV-Visible spectrophotomter. The available amount was calculated by using the standard calibration curve. [7, 9, 12, 13]

RESULT AND DISCUSSION: After the randomly selection of tablets the weight variation, friability, drug assay, disintegration and dissolution test were performed as per the United States Pharmacopoeial procedures. The result of weight variation of twenty randomly selected tablets are given in **Table 2** and **Fig. 2**.

TABLE 2: WEIGHT VARIATION TEST OF FOUR DIFFERENT BRANDS OF PARACETAMOL TABLETS

Brand A (AvgWt of Tablet =598.65 mg)			Brand B (AvgWt of Tablet =549 mg)			Brand C (AvgWt of Tablet =593.8 mg)			Brand D (AvgWt of Tablet =581.9 mg)		
Amount (mg)	Weight variation	%Weight Variation	Amount (mg)	Weight variation	% Weight Variation	Amount (mg)	Weight variation	% Weight Variation	Amount (mg)	Weight variation	% Weight Variation
603.9	5.25	0.88	542.1	6.9	1.26	594	0.2	0.03	592.5	10.6	1.82
593.2	5.45	0.91	554.2	5.2	0.95	585.9	7.9	1.33	586.5	4.6	0.79
603.6	4.95	0.83	558.5	9.5	1.73	592.7	1.1	0.19	589.7	7.8	1.34
596.2	2.45	0.41	543.4	5.6	1.02	586.7	7.1	1.20	581.1	0.8	0.14
601.3	2.65	0.44	544.3	4.7	0.86	592.5	1.3	0.22	582.2	0.3	0.05
595.1	3.55	0.59	548.5	0.5	0.10	592	1.8	0.30	574.8	7.1	1.22
600.2	1.55	0.26	547.6	1.4	0.26	588.5	5.3	0.89	585.5	3.6	0.62
599.9	1.25	0.21	545.5	3.5	0.64	601.4	7.6	1.28	557.1	24.8	4.26
595.3	3.35	0.56	551.6	2.6	0.47	588.1	5.7	0.96	594.1	12.2	2.10
597.8	0.85	0.14	546.4	2.6	0.47	603.1	9.3	1.57	590.5	8.6	1.48
599	0.35	0.06	543	6	1.09	590.6	3.2	0.54	559.1	22.8	3.92
597.9	0.75	0.13	546.5	2.5	0.46	592.4	1.4	0.24	563.9	18	3.09
601.4	2.75	0.46	550.1	1.1	0.20	598.3	4.5	0.76	582	0.1	0.02
598.6	0.05	0.01	554.8	5.8	1.06	598.2	4.4	0.74	573.1	8.8	1.51
604.6	5.95	0.10	550.5	1.5	0.27	586.7	7.1	1.20	591	9.1	1.56
598.3	0.35	0.06	552.1	3.1	0.56	607.4	13.6	2.29	599.3	17.4	2.99
593.1	5.55	0.93	549.9	0.9	0.16	591.1	2.7	0.45	556.2	25.7	4.42

598.2	0.45	0.08	548.6	0.4	0.07	599.9	6.1	1.03	592.7	10.8	1.86
597.2	1.45	0.24	556.5	7.5	1.37	597	3.2	0.54	585.6	3.7	0.64
595.8	2.85	0.48	547.6	1.4	0.26	590	3.8	0.64	594.3	12.4	2.13

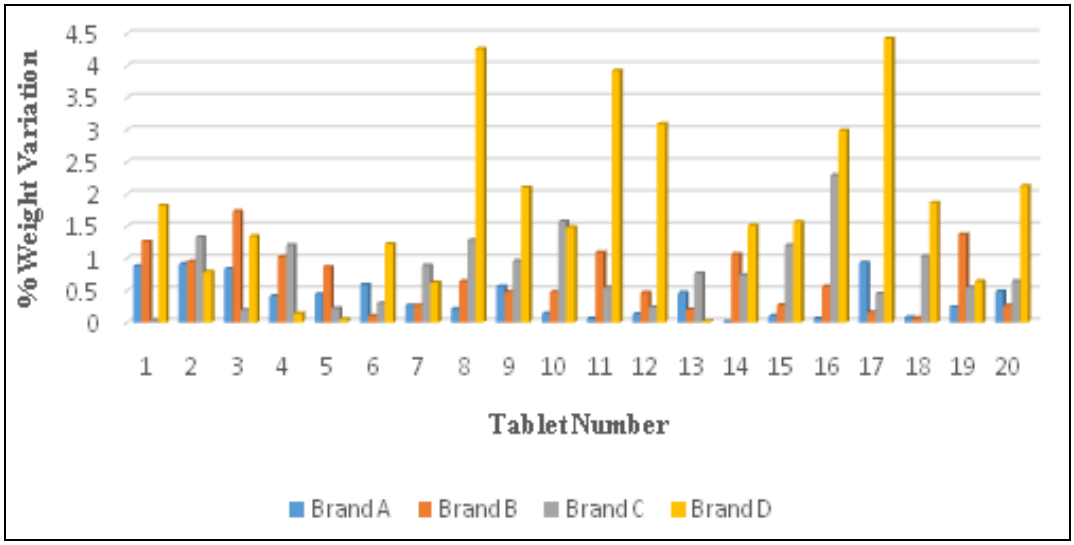

FIG. 2: WEIGHT VARIATION TEST OF FOUR DIFFERENT BRANDS OF PARACETAMOL TABLETS

As per the USP the weight variation limit for the tablet which is having the weight equal or more than 324 mg is 5 % and the given results shown that all the twenty randomly selected tablets of all four brands are having weight variation less than 5 % which proves that the four brands (A, B, C, D) of paracetamol tablets those are available in the Trinidad pharmaceutical market passed the official weight variation test. The friability test was conducted in Roche friabilator by using 10 tablets, the results of all different brands are given in the **Table 3** and **Fig. 3**.

TABLE 3: FRIABILITY TEST OF FOUR DIFFERENT BRANDS OF PARACETAMOL TABLETS

Brand	A	B	C	D
% Friability	0.39	0.41	0.52	0.19

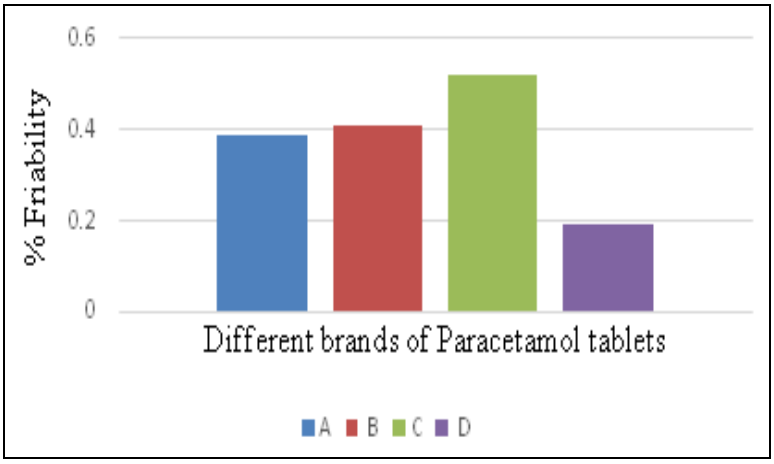

FIG. 3: FRIABILITY OF FOUR DIFFERENT BRANDS OF PARACETAMOL TABLETS

The results of friability test [7, 9] shows that all the four brands of paracetamol tablets are under the pharmacopoeia limits (1%) means all these brands of paracetamol tablets those are available in Trinidad pharmaceutical market are having good strength and can tolerate the shocks during transportation handling of these tablets. The disintegration test [7, 9] was performed in the distilled water at 37 ±2°C in the Electrolab ED-2L instrument. The results of all four brands are given in **Table 4** and **Fig. 4**.

TABLE 4: DISINTEGRATION TEST OF FOUR DIFFERENT BRANDS OF PARACETAMOL TABLETS

Brand	A	B	C	D
Disintegration Time (Minute)	1.35	5.75	0.37	1

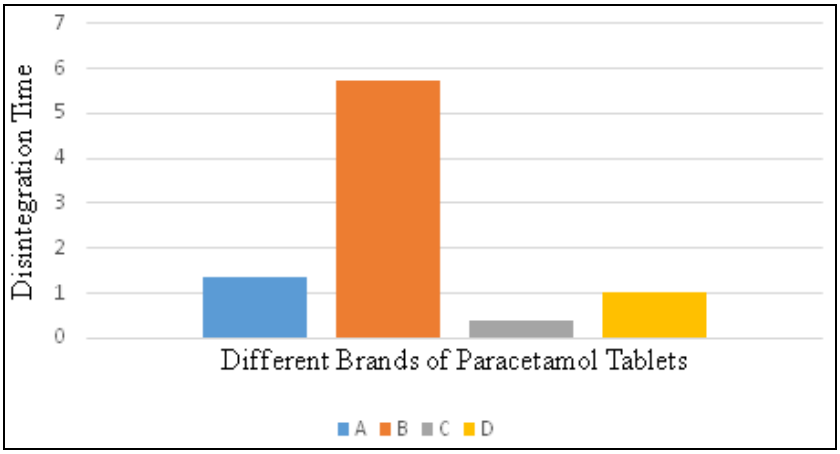

FIG. 4: DISINTEGRATION TIME OF FOUR DIFFERENT BRANDS OF PARACETAMOL TABLETS

The results of disintegration test shows that all four different brands of paracetamol tablet disintegration time is less than 6 minutes which is less than the standard disintegration time (15 minute) for uncoated tablet which proves that all these brands of paracetamol tablet passes the quality control limits as per the pharmacopoeia. The brands C disintegration time is about 37 sec means it disintegrates very fast so it might be possible that the drug will be available very fast for absorption as well as the onset of time will be very less.

To confirm the amount of paracetamol drug in the tablet drug assay was performed for all four different brands, the results are given in the **Table 5** and **Fig.5**.

TABLE 5: DRUG ASSAY OF FOUR DIFFERENT BRANDS OF PARACETAMOL TABLETS

Brand	A	B	C	D
% Drug	103.21	99.96	93.40	105.32

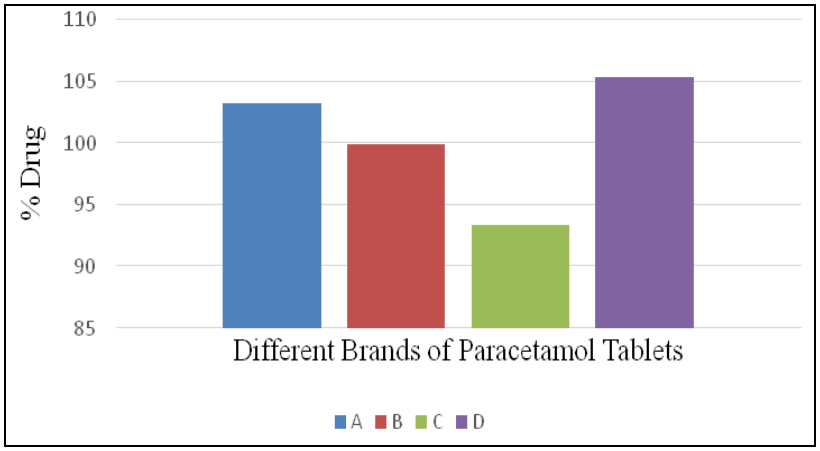

FIG. 5: DRUG ASSAY OF FOUR DIFFERENT BRANDS OF PARACETAMOL TABLETS

The results of drug assay of four different brands of paracetamol tablets shows that amount of paracetamol drug available in all these formulation is near to 100 % means drug are available as per their stated value and the dosage form is in stable form. Out of all these brands the brands D is having highest amount as compare to others but it is in therapeutic window so no chance of under and over

pharmacological action. The dissolution study was performed to see the drug release pattern in the four different brands of paracetamol tablets. The dissolution data of multipoint study are given in **Table 6** and **Fig. 6**.

TABLE 6: DISSOLUTION STUDY OF FOUR DIFFERENT BRANDS OF PARACETAMOL TABLETS

	Time (Minute)	5	10	15	30	45	60
Brand A	Amount of Drug (mg)	393.96	455.08	475.23	492.08	509.37	480.40
	Cumulative% drug release	78.79	91.02	95.05	98.42	101.87	96.08
Brand B	Amount of Drug (mg)	212.08	393.31	479.48	480.35	487.32	477.7
	Cumulative% drug release	42.42	78.66	95.90	96.07	97.46	95.56
Brand C	Amount of Drug (mg)	138.57	195.78	281.60	454.63	467.32	495.18
	Cumulative% drug release	27.71	39.16	56.32	90.93	93.46	99.04
Brand D	Amount of Drug (mg)	417.06	441.80	469.62	470.09	484.79	495.18
	Cumulative% drug release	83.41	88.36	93.92	94.02	96.96	99.04

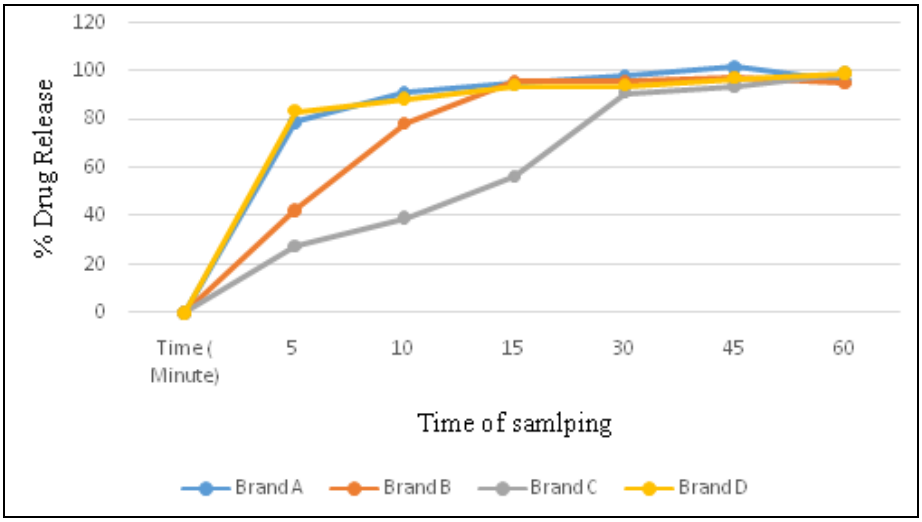

FIG 6: DRUG RELEASE STUDY OF FOUR DIFFERENT BRANDS OF PARACETAMOL TABLETS

The results of dissolution study shows that all four brands releases about 100 % drug within one hour. The brand A and D releases about 80% drug within 5 minute which means the drug the onset of action will be fast in these brands. The data proves that the dissolution study of paracetamol complies the pharmacopeia standards.

CONCLUSION: The quality control evaluations of four different brands of paracetamol tablets those are available in pharmaceutical market of Trinidad were assessed by this study. The values were compared with the standards. This study showed that all four brands (A, B, C, D) of paracetamol tablets meet the pharmacopoeia specification of different parameters. The results of various quality control parameters for tablets like weight variation, friability, disintegration time, drug assay and dissolution study all are in the pharmacopoeia limits.

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CONFLICT OF INTEREST: None

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