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Post Market In-Vitro Comparative Evaluation of Different Brands of Paracetamol

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ABSTRACT: This study evaluates the quality standards of different brands of formulations of paracetamol, which is essential to guaranteeing therapeutic efficacy. The weight fluctuations, friability, disintegration, dissolution, and pharmacopoeial assay results show compliance with the stipulated requirements. Nonetheless, differences in tablet hardness were observed. Future research may include routine analysis using HPLC techniques. The importance of quality assurance (QA) and control (QC) in pharmaceutical manufacturing is also covered in the paper. To guarantee product quality and customer satisfaction, QC actions, data collection, corrective measures, and continuous monitoring are all important. The study emphasizes how crucial efficient QC procedures are to upholding pharmaceutical quality requirements.

1. INTRODUCTION:

ISO 9000 defines Quality Control (QC) "A part of quality management focused on fulfilling quality requirements." It is a procedure or set of procedures intended to ensure that a manufactured product or performed service adheres to a defined set of quality criteria or meets the requirements of the client or customer. QC is similar to, but not identical with, quality assurance (QA).

QA is defined as a procedure or set of procedures intended to ensure that a product or service under development (before work is complete, as opposed to afterwards) meets specified requirements. QA is sometimes expressed together with QC as a single expression, quality assurance and control (QA/QC).

In order to implement an effective QC program, an enterprise must first decide which specific standards the product or service must meet. Then the extent of QC actions must be determined (for example, the percentage of units to be tested from each lot). Next, real-world data must be collected (for example, the percentage of units that fail) and the results reported to management personnel. After this, corrective action must be decided upon and taken (for

example, defective units must be repaired or rejected and poor service repeated at no charge until the customer is satisfied). If too many unit failures or instances of poor service occur, a plan must be devised to improve the production or service process and then that plan must be put into action. Finally, the QC process must be ongoing to ensure that remedial efforts, if required, have produced satisfactory results and to immediately detect recurrences or new instances of trouble[1].

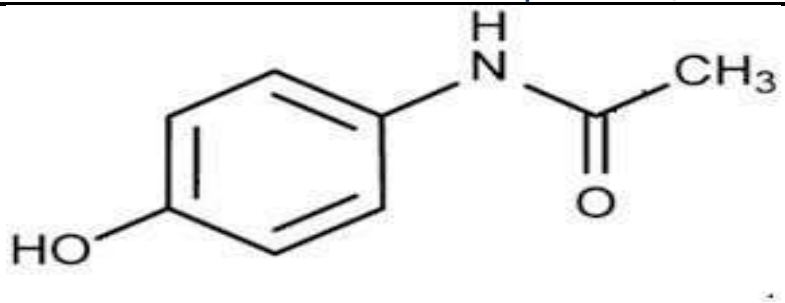
1.1 WHY IT IS NECESSARY?

It is necessary to ensure that all products sold to customers are of the highest possible quality. During quality inspections, workers check for malfunctions, discolorations, potential hazards and other defects that can compromise the quality of the merchandise.[2]

It is important because business owners must ensure they manufacture products that customers want to buy over and over again. The goal of a quality control system is to ensure that each product meets or exceeds a specific standard. A quality control system can also help business owners identify weaknesses in products and come up with solutions for improving them[3]. Paracetamol is virtually the sole survivor of the so-called “aniline derivatives” or “aniline analgesics”: acetanilide, phenacetin and paracetamol (acetaminophen). Phenacetin and paracetamol are both derivatives of acetanilide. Acetanilide was serendipitously found to possess antipyretic activity and quickly introduced into medical practice under the name of antifebrin, and was shown to possess both analgesic and antipyretic activities. But its unacceptable toxic effects, the most alarming being cyanosis due to methemoglobinemia, prompted the search of less toxic aniline derivatives. A number of compounds were tested and phenacetin (acetophenetidin) and N-acetyl-p-aminophenol (paracetamol) were found to be the most successful. Paracetamol had been synthesized by Morse in 1878 and was first used in medicine by Von Mering in 1893.[4]

1.2 CHEMISTRY OF PARACETAMOL

Chemically it is a 4-hydroxy acetanilide and an active metabolite of phenacetin, a so-called coal tar analgesic which is no longer used for medicinal purpose for its adverse effects. Paracetamol is a white, odourless crystalline powder with a bitter taste, soluble in 70 parts of water (1 in 20 boiling water), 7 parts of alcohol (95%), 13 parts of acetone, 40 parts of glycerol, 9 parts of propylene glycol, 50 parts of chloroform, or 10 parts of methyl alcohol. It is also soluble in solutions of alkali hydroxides. It is insoluble in benzene and ether. A saturated aqueous solution has a pH of about 6 and is stable (half-life over 20 years) but stability decreases in acid or alkaline conditions, the paracetamol being slowly broken down into acetic acid and p-aminophenol.



Structure of Paracetamol

Paracetamol is an over-the-counter non-steroidal anti-inflammatory drug (NSAID) which is commonly used as an analgesic and antipyretic agent but 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. The most commonly consumed daily dose, 1000mg, results in roughly 50% inhibition of both COX-1 and COX-2 in whole body blood assays ex vivo in healthy volunteers. It has been suggested that COX inhibitors might be disproportionately pronounced in the brain, explaining its anti-pyretic efficacy. It is used to relieve mild to moderate pain from headaches, muscle aches, menstrual periods, colds and sore throats, toothaches, backaches, osteoarthritis, and reactions to vaccinations (shots), and to reduce fever. Unlike opiates it is almost ineffective in intense pain and has no depressant effect on respiration. It is available in a tablet, capsule, suspension or solution (liquid), drops, extended-release (long acting) tablet, orally disintegrating tablet, suppository, intravenous, and intramuscular form. Paracetamol is generally safe and well tolerated for human use at recommended doses. It also has a low incidence of gastrointestinal side effects at therapeutic doses in contrast to the NSAIDs. But, acute over dosage can cause severe hepatic. Damage and in rare individuals, a normal dose can do the same. However, the safety and efficacy of a pharmaceutical dosage form can be guaranteed when its quality is reliable. The efficacy of pharmaceutical dosage forms generally depend on their formulation properties, and manufacturing methods, hence it is likely that the quality of dosage form may vary.[5]

1.3.MECHANISM OF ACTION

Paracetamol inhibits both isoforms COX, COX-1 and COX-2. In 2002, a COX-1 splice variant, COX-1b (later termed COX-3) was cloned from canine cerebral cortex and was shown to be sensitive to inhibition by paracetamol, but its significance in humans is uncertain. It appears likely that paracetamol is able to inhibit COX most effectively in environments where the ambient concentration of peroxides is low (for example, the brain).[6] Peripherally, and especially at sites of inflammation where the peroxide concentration is high, the action of paracetamol on COX is greatly reduced. However, in about 2005, a completely new and unforeseen mechanism of action of paracetamol was found when two independent groups, Zygmunt and colleagues and Bertolini and colleagues, produced experimental data clearly demonstrating that the analgesic effect of paracetamol was due to the potentiation of the cannabinoid/vanilloid tone in the brain and in dorsal root ganglia (indirect activation of cannabinoid CB1 receptors). In brain and spinal cord, paracetamol, following de- acetylation to its primary amine

(p-aminophenol) conjugated with arachidonic acid to form Narachidonoylphenolamine ,a compound already known as an endogenous cannabinoid , which inhibits the cellular uptake of anandamide, an endocannabinoid, and is an agonist at the vanilloid receptor TRPV1, which is believed to play a central role in nociception. The involved enzyme is fatty acid amide hydrolase.[7] AM404 is an agonist at TRPV1 receptors and an inhibitor of cellular amide uptake, which leads to increased levels of endogenous cannabinoids; moreover, it inhibits COXs in the brain, albeit at concentrations that are probably not attainable with analgesic doses of paracetamol. CB1 receptor antagonist, at a dose level that completely prevents the analgesic activity of a selective CB1 receptor agonist, completely prevents the analgesic activity of paracetamol. Thus, paracetamol acts as a pro-drug, the active one being a cannabinoid. These findings finally explain the mechanism of action of paracetamol and the peculiarity of its effects, including the behavioural ones.[8]

1.4.PHARMACOKINETICS OF PARACETAMOL

Paracetamol is well absorbed from the gastrointestinal tract following oral administration and is not subject to significant first-pass metabolism in the liver, with oral bioavailability estimated at between 63–89% in adults. However, drug-food interaction tends to slow the rate of absorption of paracetamol, while caffeine accelerates absorption. Prokinetic drugs (such as metoclopramide) accelerate gastric emptying, enhancing the rate of absorption, while drugs that decrease the rate of gastric emptying (e.g. morphine) slow absorption, and in some cases prevent attainment of therapeutic plasma levels. Rectal absorption of paracetamol is slower and less predictable, with bioavailability between 24% and 98%. This variability depends on the size, physical composition and number of suppositories used, and on the rectal pH. Paracetamol is not significantly bound to plasma proteins, and has a volume of distribution of 0.7–1 l.kg−1. It is non-ionised at physiological pH and freely crosses the placenta and blood–brain barrier. Intravenous paracetamol is also available as the pro-drug propacetamol, though this has never held a license in the UK. One gram of paracetamol provides 0.5 g paracetamol after hydrolysis, and bioequivalence has been established.[9]

The minimum plasma paracetamol level required for analgesia and antipyresis is thought to be 10µg/ml, and although not clearly deined, the therapeuticrange is usually stated to be 10–20µg/ml. 150µg/ml is consideredto be the threshold for potential hepatotoxicity. Maximal analgesic and antipyretic activity occurs 1–2 hr after peak plasma levels, and the time to achieve this varies with the route of administration. Peak plasma concentration (C.max) is achieved Approximately 45 min after 1 g orally, at between 3.5 and 4.5 h after rectal administration of both 20 and 40 mg/kg andapproximately25min after a 1g intravenous infusion. Cerebrospinal fluid levels lag behind those seen in plasma, with an equilibration half-time of 72 hr.

1.5.METABOLISM OF PARACETAMOL

Metabolism of paracetamol occurs primarily in the liver, while elimination occurs almost entirely through the kidney. Following absorption of therapeutic doses, approximately 90% is metabolised by glucuronidation and sulphonation to form non-toxic metabolites, which are excreted in the urine. A small fraction undergoes oxidation

by the cytochrome P450 system to form the highly reactive metabolite N-acetyl-p- benzoquinoneimine (NAPQI).[10]

NAPQI reacts with glutathione, forming conjugates that are subsequently excreted in urine. Following the ingestion of large amounts of paracetamol, hepatic glutathione is depleted and NAPQI accumulates, leading to sub-acute hepatic necrosis, and in severe cases, to hepatic failure. Clearance is lowest in neonates, with values rising through childhood. Elimination half-life is 2-4 h in normal adults, increasing to 4-5 h in new born and to 11 h in premature infants. One to four percent is excreted unchanged in the urine, and an increased dose interval of 6-8 h is recommended in patients with severe renal impairment.[11]

1.6.DOSE OF PARACETAMOL

In general, children's dosages vary with the age of the child and the type of product, therefore the instructions on the pack should always be followed (table 1). In general, children's dosages are based on a single dose of 10mg paracetamol per kilogram bodyweight, which can be repeated 46 hourly, not exceeding four doses per 24 hours.[12]

Table 1: Dose of the Paracetamol for the Adult and the Children

Age group	Dose
Adult	Two 500mg tablets (i.e., 1gm paracetamol) every four to six hours, not exceeding eight tablets (4gms) in any 24 hour period.
Children	**a) 2 month old child:** single dose of 60mg (i.e. 2.5mL paracetamol liquid (oral suspension) at a strength 120mg/5 mL). Paracetamol may be given on a doctor's recommendation only following immunization.
	b) Under 3 months: 10mg paracetamol per kilogram body weight (5mg/kg if jaundiced), on a doctor's advice only.
	c) 3 months to 1 year: Between 60mg and 120mg (i.e. 2.5mL to 5mL of paracetamol liquid (oral suspension) at strength of 120mg/5mL) may be repeated every 4-6 hours to a maximum of 4 doses in 24 hours.
	d) 1 to 5 years: 120mg to 250mg (i.e. 5mL to 10mL of paracetamol liquid (oral suspension) at a strength of 120mg/5mL) may be repeated every 4-6 hours to a maximum of 4 doses in 24 hours.
	e) 6 to 12 years: 250mg to 500 mg (i.e. 5mL to 10mL paracetamol liquid (oral suspension) at a strength of 250mg/5mL) may be repeated every 4-6 hours to a maximum of 4 doses in 24 hours.

(Paracetamol Information Centre, n.d.b)

1.7.MEDICAL USES

Fever

Paracetamol is used for reducing fever in people of all ages.[13] The World Health Organization recommends that paracetamol be used to treat fever in children only iftheir temperature is higher than 38.5 °C (101.3 °F).[14] The efficacy of paracetamol by itself in children with fevers has been questioned and a meta-analysis showed that it is less effective than ibuprofen.[15]

Pain

Paracetamol is used for the relief of mild to moderate pain. The use of the intravenous form for short-term pain in people in the emergency department is supported by limited evidence.[16]

Osteoarthritis

Paracetamol has relatively little anti-inflammatory activity, unlike other common analgesics such as the nonsteroidal anti-inflammatory drugs (NSAIDs) aspirin, and ibuprofen, but ibuprofen and paracetamol have similar effects in the treatment of headache. Paracetamol can relieve pain in mild arthritis, but has no effect on the underlying inflammation, redness, and swelling of the joint. It has analgesicproperties comparable to those of aspirin, while its anti-inflammatory effects are weaker. It is better tolerated than aspirin due to concerns about bleeding with aspirin.[17]

Lower back

Based on a systematic review, paracetamol is recommended by the American Pain Society as a first-line treatment for low back pain. In contrast, the American College of Physicians found good evidence for NSAIDs but only fair evidence for paracetamol, while other systematic reviews have concluded that evidence for its efficacy is lacking entirely.[18]

Headaches

A joint statement of the German, Austrian, and Swiss headache societies and the German Society of Neurology recommends the use of paracetamol in combination with caffeine as one of several first-line therapies for treatment of tension or migraine headache. In the treatment of acute migraine, it is superior to placebo, with 39% of people experiencing pain relief at 1 hour compared with 20% in the control group.[19]

Post - operative

Paracetamol combined with NSAIDs may be more effective for treating postoperative pain than either paracetamol or NSAIDs alone.[20]

Teeth

NSAIDs such as ibuprofen, naproxen, and diclofenac are more effective than paracetamol for controlling dental pain or pain arising from dental procedures; combinations of NSAIDs and paracetamol are more effective than either alone.[21] Paracetamol is particularly useful when NSAIDs are contraindicated due to hypersensitivity or history of gastrointestinal ulceration or bleeding.[22] It can also be used in combination with NSAIDs when these are ineffective in controlling dental pain alone. The Cochrane review of preoperative analgesics for additional pain relief in children and adolescents shows no evidence of benefit in taking paracetamol before dental treatment to help reduce pain after treatment for procedures under local anaesthetic, but the quality of evidence is low.[23]

Other

The efficacy of paracetamol when used in combination with weak opioids (such as codeine) improved for about 50% of people, but with increases in the number experiencing side effects.[Combination drugs of paracetamol and strong opioids such as morphine improve analgesic effect.[24]

The combination of paracetamol with caffeine is superior to paracetamol alone for the treatment of common pain conditions, including dental pain, post partumpain, and headache.[25]

2. AIM AND OBJECTIVE

The study aim is to analyse the different brands of paracetamol 500mg tablets for its quality by performing weight variation, Hardness, friability, disintegration, Pharmacopoeial assay and dissolution test.

3. PLAN OF WORK

Literature survey.

Procurement of different brands of paracetamol from market. Evaluation Parameters

- General appearance : Size, Thickness, Diameter, Shape, Colour, Odour, Surface texture
- Determination of Weight variation
- Determination of Hardness
- Determination of Friability
- Determination of Disintegration
- Pharmacopoeial assay
- Determination of Dissolution

4. EXPERIMENTAL

4.1. Material

Apparatus and Equipments

Double beam UV-Visible Spectrophotometer (Systronic's Model no: 2201), Analytical balance (Electric precision balance, Model no.:3003), Hardness Tester (Monsanto, Mht-20), Tablet Friability Tester (Roche, FTV-2), Disintegration apparatus (ED-2L), Dissolution apparatus (EDT-08LX) and Ultrasonicator (Toshcon, SW 4).

Chemicals and reagent

To perform the study paracetamol tablets of four different brands (Calpol, Merimol, Pyrekem, Pacimol)were purchased from Shree Sai Medical Store, Mahadula,Nagpur, Maharashtra and coded as A, B, C and D respectively. All paracetamol brands were labeled to contain 500 mg of paracetamol per tablet. Buffer solution PH 5.8 were made fresh by using Sodium dibasic, sodium monobasic, Distilled water at Sonekar College of Pharmacy, Mahadula, Koradi, Nagpur.

4.2 Method

Evaluation of Tablets[26] General Appearance

The general appearance of tablet was done by visual identification for elegance, shape, colour, surface texture.

Thickness

The thickness of the tablets was determined by using vernier callipers. Randomly 10 tablets were selected and used for determination of thickness. The result was expressed in Mean and unit in mm.

Diameter

The diameter of the tablets was determined by using vernier callipers. Randomly 10 tablets were selected and used for determination of thickness. The result was expressed in Mean and unit in mm.

Weight variation

20 tablets were taken and were weighed using analytical balance machine. Their average weight was calculated. Then each tablet was weight and their % deviation and standard deviation from the average weight was determined.

$$\% \text{ Deviation} = \frac{W_{avg} - W_{ind}}{W_{avg}}$$

Where,

W_{avg} = Average weight of tablets W_{ind} = Individual weight of tablet

Hardness

A tablet was placed vertically on the Monsanto hardness tester. The load was then applied along the radial axis of the tablet. The weight or load required for breaking the tablet was noted down. Similarly it was done for 10 tablets.

Friability

5 tablets were weighed and placed in Roche friability apparatus. The apparatus was rotated at a speed of 25 rpm for 4 mins. The tablets were then again weighed and was compared with the initial weights. The percentage friability was calculated using the formula.

$$\% F = 1 - \frac{W \times 100}{Wo}$$

Where,

% F = Friability in percentage, Wo = Initial weight of tablets,

W = Weight of the tablets after revolution.

Tablet Disintegration:

Disintegration test was performed using USP disintegration device. 6 tablets were placed in disintegration test apparatus at temperature of 37 ± 0.2^{O}C containing simulated gastric fluid (Buffer solution PH 5.8). The time taken for tablets to disintegrate was noted down.

Pharmacopoeial Assay (I.P) :

20 tablets from each brand of paracetamol was weighed using analytical balance and finely powdered an accurately weighed portion of powder equivalent to 150mg paracetamol were transferred to a 200ml volumetric flask to it 50 ml of 0.1M sodium hydroxide (NaOH) and 100ml of distilled water was added and sonicated for15 minutes and diluted up to 200ml and filtered. 10ml of the filtrate was transferred to100ml volumetric flask and further diluted to 100ml with distilled water and the absorbance of resulting mixture was taken at 257nm the drug content was calculated by taking A (1%, 1cm) as 715 at the maximum 257 nm.

Tablet Dissolution :

Dissolution test was done by using test U.S.P. Type- 1 (Basket) Single flask Dissolution Apparatus. Gastric Fluid was taken as a Dissolution Medium. The tablets were immersed into 900 ml, of dissolution medium. The temperature of the dissolution medium was maintained at 37 ± 0.2^{O}C. The basket was rotated at a speed of 50 rpm. After an interval of every 15 minutes, 2 ml. of the medium was pipette out and replaced with fresh medium (Buffer PH 5.8), and continued for 60mins. The pipetted out samples were then diluted to 10 ml, with fresh

dissolution medium and were then filtered. The absorbance of the filtered samples was taken using U.V. Spectroscope at λmax 257nm and 243nm.The % drug release of each brand of paracetamol tablet was calculated by using standard calibration curve method.

5. Result and Discussion General appearance

The parameter like shape, colour, odour, and surface texture were studied by visual identification while thickness and diameter was measured using vernier calliper.

The results are shown in **Table 2.**

Table 2: Comparative study of General appearance of different brands of Paracetamol tablets.

Sample	Thickness (mm)	Diameter (mm)	Shape	Colour	Odour	Surface texture
A	4	12	Rounded	White	Odourless	Smooth
B	4	13	Rounded	White	Odourless	Smooth
C	4	13	Rounded	White	Odourless	Smooth
D	5	13	Cylindrical	White	Odourless	Smooth

Weight Variation

Tablets are required to meet a weight variation test were the active ingredient comprises a major portion of the tablet and were control of weight may be presumed to be an adequate control of drug content uniformity. 20 tablets were taken and weighed, their average weight was calculated. The results are shown in **Table 3.**

Table 3 : Weight Variation data of different paracetamol brand tablets.

Sr. no.	Weight of individual tablets (gm.)			
	A	B	C	D
1.	0.540	0.577	0.564	0.598
2.	0.539	0.580	0.570	0.615
3.	0.546	0.581	0.562	0.600
4.	0.531	0.565	0.568	0.612

5.	0.533	0.583	0.566	0.605
6.	0.537	0.571	0.572	0.603
7.	0.540	0.574	0.566	0.602
8.	0.532	0.579	0.556	0.609
9.	0.533	0.577	0.560	0.601
10.	0.555	0.575	0.563	0.608
11.	0.546	0.572	0.564	0.606
12.	0.541	0.587	0.559	0.606
13.	0.542	0.590	0.562	0.605
14.	0.529	0.573	0.563	0.610
15.	0.543	0.587	0.564	0.599
16.	0.533	0.580	0.572	0.606
17.	0.539	0.567	0.568	0.603
18.	0.527	0.581	0.564	0.606
19.	0.534	0.585	0.563	0.598
20.	0.536	0.595	0.567	0.600
Mean±SD	0.537±0.0067	0.578±0.0076	0.578±0.0040	0.578±0.0047

All the four brands of paracetamol (500 mg) showed a percentage weight variation within the range of ±5 and, therefore, comply with the specification of USP.

Hardness

Tablets require a certain amount of strength, or hardness to withstand the mechanical shocks of handling and transportation yet soft enough to be able to disintegrate properly after swallowing. Since there is also a relationship between hardness and disintegration rate of the tablets, it is essential that the hardness of the tablets are within the acceptable range. Tablets with increased hardness values tend to have increasing disintegration time. Hardness test was done by using Monsanto hardness tester. The results are shown in **Table 4.**

Table 4 : Hardness of tablet

Sample	**Hardness(kg/cm^2)**

A	5.2
B	4.3
C	2.7
D	5.1

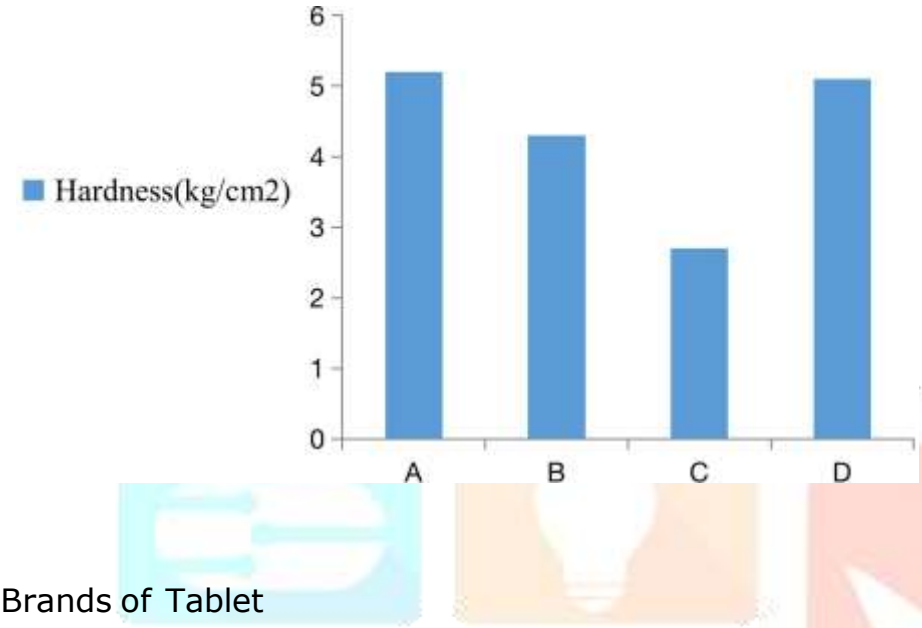


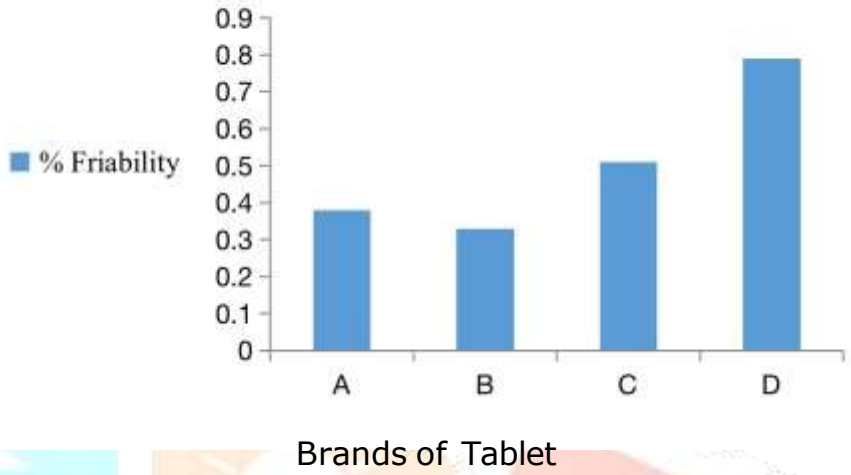
Figure 1 : Comparative study of Hardness of different brands of tablets

In the study, it was found that both B and C brands of paracetamol group passed the test of tablet crushing strength or hardness. Both these brands have acceptable crushing strength of between 4 kg/cm^2 to 10 kg/cm^2.

Friability

Tablets should have the ability to resist abrasion when they are subjected to stresses from collision and tablet sliding towards one another and other solid substances, which can result in the removal of small fragments and particles from the tablet surface. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable and any broken or smashed tablets are not picked up. The friability test was performed by using Roche friabilator with 5 tablets of each brand of paracetamol tablet. The results obtained are represented in **Table 5** and **Figure 2.**

Figure 2: Comparative study of Friability test of different brands of paracetamol tablets



Sample	Initial Weight (gm.)	Final Weight (gm.)	Wo-W (gm.)	%Friability
A	2.692	2.682	0.010	0.38
B	2.430	2.422	0.008	0.33
C	2.393	2.381	0.012	0.51
D	2.531	2.517	0.014	0.79

Table 5: Friability of tablet

All the four brands of paracetamol have passed the friability test and have meet the specification of USP which specifies that the friability study must not lose 1% of their initial weight.

Pharmacopoeial Assay

Test for percentage of content is based on the assay of the individual content of active ingredient of a number of single dose units. The IP, USP and BP specifications for assay are that the paracetamol contents should not be less than 90 and not more than 110.

The drug content was calculated by Assay is a test carried out for the purpose of estimating the potency of material preparation or pooled result of 2 or more such test which pharmacopoeia depend. In this study the assay was performed on different brands of paracetamol tablet in compliance to IP to asses % content of paracetamol. IP

specific the content of paracetamol to be between 95-105% of stated amount. The result for assay of paracetamol were shown in **Table 6.**

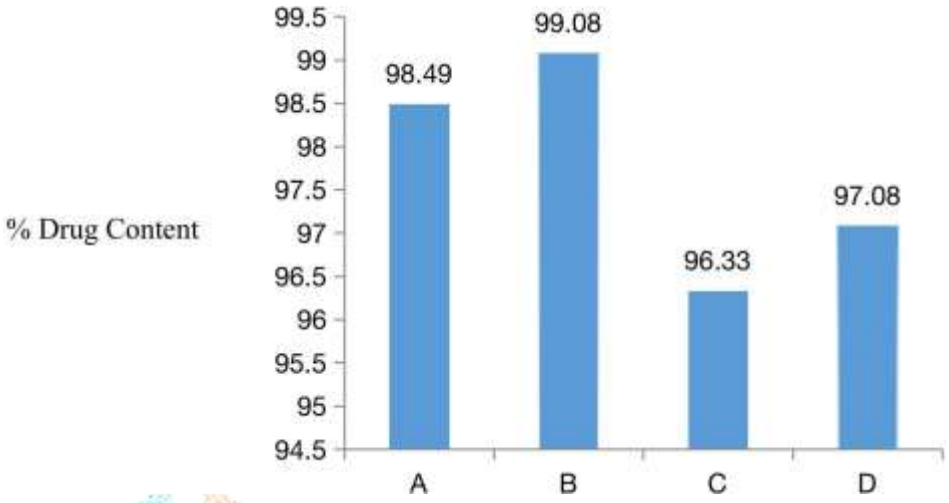


Figure 3 : Comparative study of Pharmacopoeial assay of different brands of paracetamol tablets.

Table 6: Drug Content of tablet

Sample	% Drug Content
A	98.49
B	99.08
C	96.33
D	97.08

All brands, contained the paracetamol within 100 ±10 % of the label claim. Therefore, the assay results ascertain the presence and compential quality of the drug in all products.

Disintegration

Disintegration is essential for better bioavailability which results in better absorption and consequently better therapeutic action. The effectiveness of a drug is related to its disintegration time. Disintegration time may vary considering to its disintegrator used. Disintegration for test 6 tablets were selected and placed in disintegration test apparatus. The time taken for disintegration of tablet was recorded in **Table 7** and **Figure 3.**

Table 7: Disintegration time of tablets

Sample	Time required to disintegrate (min.sec)
A	0.34
B	2.20
C	1.24
D	3.47

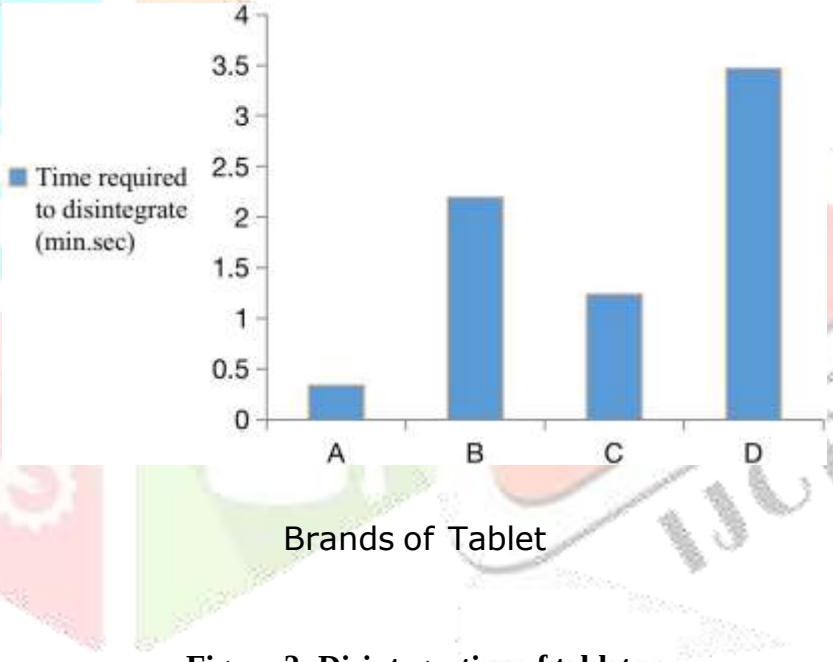


Figure 2: Disintegration of tablets

All the four brand of Paracetamol have a disintegration time that is within the acceptable range and have met the specification of USP where a majority of the tablets have a maximum disintegration time was found to be within 30 minutes.

Standard Calibration Curve :

Different solution were prepared of increasing concentration and the result are tabulated in **Table 8.**

Table 8: Standard Calibration curve

Sr.No.	Concentration (µg/ml)	Absorbance
1.	5	0.262
2.	10	0.411
3.	15	0.588
4.	20	0.745
5.	25	0.891
6.	30	1.049
7.	35	1.205
8.	40	1.325

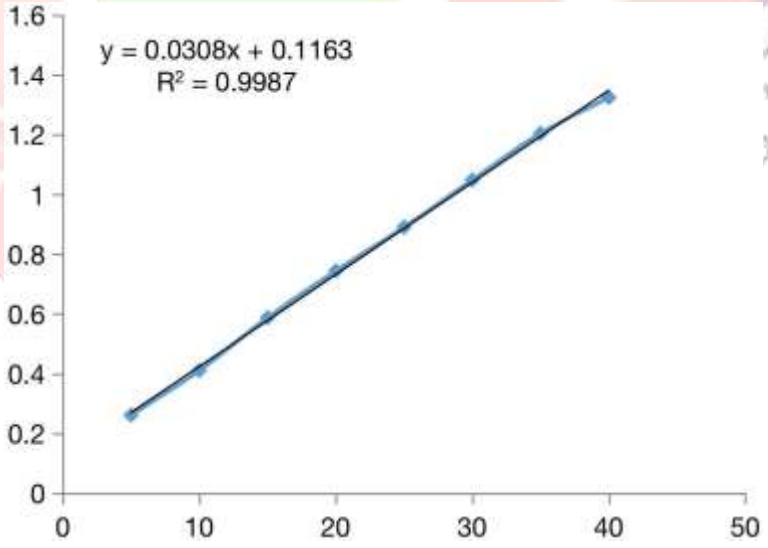


Figure 3: Standard calibration curve

Dissolution :

Dissolution profile of four brands was performed, to provide information regarding biological bioavailability and brand to brand consistency. A dissolution test was intended to determine the percent release of the samples in 60 minutes and the results are shown in **Table 9**.

Table 9: Comparative study of dissolution of different brands of paracetamol tablets. Comparative study of dissolution of different brands of paracetamol tablets.

Sr. No.	Time (min)	A		B		C		D	
		Abs.	%drug release	Abs.	%drug release	Abs.	%drug release	Abs.	%drug release
1.	5	0.530	24.17	0.521	23.65	0.502	22.54	0.521	23.65
2.	10	0.732	35.98	0.699	34.05	0.695	33.82	0.723	35.45
3.	15	0.992	51.17	0.835	42.00	0.885	44.92	0.987	50.88
4.	20	1.201	63.39	1.085	56.61	1.099	57.43	1.101	57.54
5.	30	1.395	74.72	1.301	69.23	1.283	68.18	1.325	70.63
6.	45	1.678	91.26	1.592	86.24	1.596	86.47	1.612	87.41
7.	60	1.805	98.69	1.789	97.75	1.799	98.33	1.801	98.45

Thorough evaluation, highest percent release concentration was found in Sample A, (98.69 %) while the lowest percent release concentration was recorded in sample B (97.75%).

6. Summary

- Branded products of paracetamol is collected from market and various test on various parameters were performed by using suitable quality control tests like appearance, weight variation, hardness, friability, drug content, disintegration and dissolution indicate that values were within permissible limit for all tablets.
- Tablets are required to meet a weight variation test as the active ingredient comprises a major portion of the tablet and control of weight may be presumed to be an adequate control of drug content uniformity. 20 tablets were taken and weighed, their average weight was calculated. All the four brands of paracetamol (500 mg) showed a percentage weight variation within the range of ±5 and, therefore, comply with the specification of USP.
- Tablets require a certain amount of strength, or hardness to withstand the mechanical shocks of handling and transportation yet soft enough to be able to disintegrate properly after swallowing. Since there is also a relationship between hardness and disintegration rate of the tablets, it is essential that the hardness of the tablets are within the acceptable range. Tablets with increased hardness values tend to have increasing disintegration time. Hardness test

was done by using Monsanto hardness tester. The study showed all brands of paracetamol group passed the test of tablet crushing strength or hardness and have acceptable crushing strength of between 4 kg/cm^2 to 10 kg/cm^2.

- The friability test was performed by using Roche Friabilator with 5 tablets of each brand of paracetamol tablet. All the four brands of paracetamol have passed the friability test and have meet the specification of USP.
- Disintegration is essential for better bioavailability which results in better absorption and consequently better therapeutic action. The effectiveness of a drug is related to its disintegration time. The time taken for disintegration of tablet was recorded. All the four brand of Paracetamol have a disintegration time that is within the acceptable range and have met the specification of USP where a majority of the tablets have a maximum disintegration time was found to be within 30 minutes.
- Dissolution profile of four brands was performed, to provide information regarding biological bioavailability and brand to brand consistency. A dissolution test was intended to determine the percent release of the samples in 60 minutes.
- Assay is a test carried out for the purpose of estimating the potency of material In this study the assay was performed on different brands of paracetamol tablet in compliance to IP to asses % content of paracetamol. IP specific the content of paracetamol to be between 95-105% of stated amount. The result for assay of paracetamol.

7. Conclusion

Paracetamol is a well-established and proven analgesic and antipyretic drug. Therapeutic response of any formulation depends on its quality parameter. From the study it was identified that all the finished products tests like weight variations, hardness, friability, Pharmacopoeial assay, disintegration, dissolution of all paracetamol brands complied the specification. Variations was obtained in Hardness of tablets. Further studies could also include the HPLC method for routine analysis of paracetamol in bulk as well as in pharmaceutical dosage formulation.

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