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Comparative Study of Generic Brand and Different Multinational Brands of Paracetamol

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ABSTRACT

Using standard analytical techniques as per pharmacopoeial guidelines, this study intends to evaluate key parameters including weight variation, hardness, friability, disintegration time, and dissolution profile to assess their pharmaceutical equivalency and ensure the safety and efficacy of both local and multinational brands available in the market, comparing the quality of locally manufactured paracetamol tablets against those produced by multinational pharmaceutical companies.

Paracetamol (PCT) is one of the most widely used over-the-counter (OTC) drugs among patients, and paracetamol pills are marketed by numerous vendors worldwide. As an analgesic and antipyretic , paracetamol is often and extensively used. In this study we examine and evaluate the assessment parameters of the different brands of paracetamol pills sold in the Indian state of Maharashtra. In this study, five distinct brands of paracetamol were used. These brands are randomly sampled from various pharmacies. The study was entirely experimental and evaluated the in vitro quality of paracetamol tablets using various analytical methods and procedures in accordance with BP, USP, and other official publications. (PCT) is one of the most widely used over-the-counter (OTC) drugs among patients, and paracetamol pills are marketed by numerous vendors worldwide. As an analgesic and antipyretic , paracetamol is often and extensively used. In this study we examine and evaluate the assessment parameters of the different brands of paracetamol pills sold in the Indian state of Maharashtra. In this study, five distinct brands of paracetamol were used. These brands are randomly sampled from various pharmacies. The study was entirely experimental and evaluated the in vitro quality of paracetamol tablets using various analytical methods and procedures in accordance with BP, USP, and other official publications.

Keywords Paracetamol, analgesic and antipyretic, evaluation parameters, weight variation test, hardness test, friability test, disintegration test, dissolution test.

INTRODUCTION

1 History

The acylated aromatic amide known as paracetamol (PCT) was first used in medicine by Von Mering in 1893 as an antipyretic and analgesic. It has been used as a home remedy for more than 30 years and is widely acknowledged as a highly successful treatment for fever and pain in both adults and children. In many nations, it is the most commonly used medication as a substitute for aspirin and phenacetin, second only to acetylsalicylic acid. PCT, commonly referred to as acetaminophen (N-acetyl-p-aminophenol, 4-acetamidophenol), is a common component of many prescription analgesics and cold and flu remedies. Although typical dosages of it are surprisingly safe, intentional or unintentional overdoses are prevalent due to its widespread availability.Since PCT lacks anti-inflammatory qualities, it does not belong to the class of medications known as non-steroidal anti-inflammatory medicines, or NSAIDs, which includes aspirin and ibuprofen, two typical analgesics.PCT has no effect on the fetal ductus arteriosus, renal function, blood coagulation, or stomach lining irritation. Similar to NSAIDs, PCT has not been shown to produce euphoria or change mood in any manner, unlike opioid medications.One advantage of NSAIDs and PCT is that they don't carry the danger of addiction, dependency, tolerance, or withdrawal. Physical, chemical, and biological property data are readily accessible[1].

2 Drug Profile

Paracetamol is a non-steroidal anti-inflammatory drug (NSAID) that is commonly used as an analgesic and antipyretic agent on a global scale. However, it has weak anti-inflammatory effects due to its inability to inhibit cyclooxygenase (COX) in the presence of high concentrations of peroxides, which are present at sites of inflammation.It comes in a variety of forms, including tablets, capsules, liquid suspensions or solutions, drops, oral disintegrating tablets, extended-release (long-acting) tablets, suppositories, intravenous, and intramuscular. At recommended dosages, paracetamol is typically safe and well tolerated for human use. Compared to NSAIDs, it also has a lower frequency of gastrointestinal adverse effects at therapeutic dosages.However, in rare cases, a typical dose can also result in significant liver damage, as can acute overdosing. However, when a pharmaceutical dosage form's quality is dependable, its safety and effectiveness can be assured. Since the formulation characteristics and manufacturing processes of pharmaceutical dosage forms typically determine their effectiveness, it is probable that the dosage form's quality may differ[2].

3 Physiochemical Property's

As illustrated in the figure, paracetamol, often known as acetaminophen, is a 4-hydroxy acetanilide and an active metabolite of phenacetin, a so-called coal tar painkiller that is no longer utilized for medical purposes due to its negative side effects. A white, odorless, crystalline powder with a bitter taste, paracetamol dissolves in 70 parts water (1 in 20 boiling water), 7 parts 95% alcohol, 13 parts acetone, 40 parts glycerol, 9 parts propylene glycol, 50 parts chloroform, or 10 parts methyl alcohol. Moreover, it dissolves in alkali hydroxide solutions. It is insoluble in ether and benzene.With a pH of around 6, a saturated aqueous solution is stable (half-life of 20 years), but stability declines in acidic or alkaline environments as the paracetamol gradually breaks down into acetic acid and p-aminophenol[3].

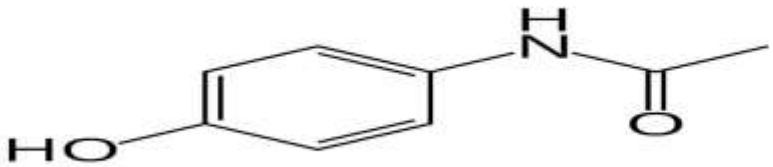

Fig. Acetaminophen

4 Bioavailability Facts

When taken orally, paracetamol is readily absorbed from the digestive system and does not undergo much first-pass metabolism in the liver; in adults, its oral bioavailability is estimated to be between 63 and 89% (Oscier& Milner, 2009). But whereas caffeine speeds up absorption, drug-food interactions tend to cut down paracetamol's rate of absorption. Prokinetic medications (like metoclopramide) speed up stomach emptying and increase absorption, whereas medications that impede stomach emptying (like morphine) slow absorption and can make it impossible to reach therapeutic plasma levels.With a bioavailability ranging from 24% to 98%, rectal absorption of paracetamol is slower and less consistent (Oscier& Milner, 2009). This fluctuation is dependent on the rectal pH, suppositories' size, physical makeup, and quantity consumed[2,3].

Paracetamol

We take a number of medications on a regular basis without understanding their composition, toxicity, or mode of action. One of these, paracetamol or acetaminophen, is typically used to treat fever, headaches, and certain ailments. This medication's chemical name is N-acetyl-para-aminophenol.Paracetamol is commonly used for its antipyretic and analgesic activities.It is used to treat a variety of mild-to-moderate pain conditions, including minor arthritis pain, headaches, sprains, colds, flu, and dysmenorrhea. Through this route, nonsteroidal anti-inflammatory medications (NSAIDs) work by preventing prostaglandin (PG) synthesis.Paracetamol is typically thought to be a weak suppressor of PG formation. Additionally, it lowers PG levels in vivo.When taken as directed, paracetamol is safe. Any medication taken at the right dosage actually has no major negative side effects. But long-term use of any substance or overdoses can have negative effects, particularly on the liver.Overdosing on paracetamol can have major negative effects on the human body. The organ most frequently implicated in acute paracetamol poisoning is the liver. About 90% of the paracetamol is removed in the urine as sulfate and glucuronide conjugates after being extensively digested by the liver. Overdosing on paracetamol can cause hepatotoxicity, which damages the liver and is a prevalent cause of poisoning globally. Furthermore, high dosages of this medication increase the risk of problems such as stomach bleeding in the upper gastrointestinal tract.Kidney is the second target organ of paracetamol toxicity.Heavy paracetamol use (300 grams per year on average, or 1 gram daily) has been linked to a disorder called "Small Indented and Calcified Kidneys" (SICK)[4].

A pharmaceutical dosage form's safety and effectiveness can be ensured when its quality is consistent. Pharmaceutical dosage form quality may vary since formulation characteristics and manufacturing processes often determine how effective a dosage form is[5].

The process of creating solid dosage forms includes processing multiparticulate powders with varying sizes, shapes, and distributions. A powder bed's individual medication particles differ greatly in size, shape, and distribution. A powder bed's particle size and dispersion are crucial factors to take into account while filling capsules or compacting them into tablets.Practically speaking, every solid dosage form used in pharmacies must eventually be treated as a powder, and how the powder is handled is significantly impacted by its flow. It is impossible to overstate the significance of consistent flow characteristics of powder or granules from the hopper to the machine's die.The process of adding a granulating (binding) fluid to powdered particles causes them to aggregate, adhere, or have cohesive properties, forming regular, bigger multiparticulate entities known as granules. Granulation of drug particles is typically done to give the tablet formulation cohesiveness and to enhance the flow characteristics of the individual particles in order to improve the poor compression properties that are already present and to avoid constituent segregation, which may be primarily caused by differences in size or density.When manufacturing tablets, the size of the particles prior to compaction is a crucial factor that is frequently overlooked. Whether a decrease or an increase in particle size will affect the mechanical properties of tablets is uncertain. Important factors influencing the mechanical characteristics of compressed compacts include tablet bond strength and capping/lamination tendency as determined by tensile strength (T) and the brittle fracture index

(BFI). Additionally examined were the effects of particle size distribution on the tablets' porosity, tensile strength, packing fraction, and friability characteristics[6].

A pharmaceutical dosage form's safety and effectiveness can be ensured when its quality is consistent. The following factors should be taken into account while validating a tablet: weight variation, homogeneity of content, thickness, hardness, friability, disintegration, and dissolution. Additionally, quality control parameters and tablet physical characteristics are helpful instruments for preserving consistency in batch-to-batch manufacturing, and they have to be carried out for each and every pharmaceutical product. Each of these variables affects drug absorption, bioavailability, and other aspects and is intimately connected to the others.Because standard quality requirements are necessary for higher-quality medication, the study's objective was to compare the quality control parameters of different brands of tablets in a formulation[7].

1 Dose of Paracetamol in adult and children[8]

Age group dose

It is recommended to take two 500mg tablets (one gram of paracetamol) every four to six hours, with a maximum of eight tablets (4 grams) in a 24-hour period.

A) 2 Month child-

60 mg taken once, which is equivalent to 2.5 mL of oral suspension of paracetamol at a dosage of 120 mg/5 mL. On a doctor's advice, paracetamol should only be administered after vaccination.

B) Under 3 Month-

10mg paracetamol per kilogram body weight (5mg/kg if jaundiced), on a doctor's advice only.

C) 3 Month 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 Year to 5 Year-

120mg to 250mg (i.e. 5mL. to 10mL 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.

E) 6 Year to 12 Year-

250 mg to 500 mg (or 5 to 10 mL of oral solution of 250 mg/5 mL of paracetamol) can be taken every 4–6 hours for a maximum of 4 doses in a 24-hour period.

Materials and Methods

1 MATERIALS

Every chemical and reagent utilized is of laboratory quality. An academic organization provides all chemicals, reagents, and logistical assistance. The British Pharmacopoeia and the United States Pharmacopoeia served as the working standards for the experimental research project. We bought and gathered four international brands and one generic or local brand of paracetamol compressed tablets (TABLE 1) from a pharmacy[9].

The pharmaceutical tablet's effectiveness and safety should be ensured by performing quality control tests such as the weight variation, disintegration, friability, dissolution, and hardness tests. We randomly purchased ten tablets from a pharmacy or medical store that had the same batch number and were labeled to contain 500 mg of paracetamol[9].

The same procedure for each test was applied in each brand.

Table 1. Four Multinational Brands & One Generic or Local Brands Of Compressed Tablets Of Paracetamol.

Sr.No.	Brands	Labelled As
1	Generic Brand	TABLET A
2	Multinational Brand A	TABLET B
3	Multinational Brand B	TABLET C

4	Multinational Brand C	TABLET D
5	Multinational Brand D	TABLET E

A) STUDY DESIGN

We compared the in vitro quality control parameters of the commercially available paracetamol tablet brands by analyzing the pharmacopoeial assay, weight variation, hardness, friability, disintegration time, and dissolution profile. Several test procedures related to evaluating the quality of tablets were carried out as part of the study[10].

B) SAMPLE COLLECTION

Tablets of paracetamol from various manufacturers were bought from the pharmacy to conduct the investigation. It was stated on the label that each of the paracetamol tablet brands contained 500 mg of the drug. The tablets were taken for evaluation prior to two years of the indicated expiration date, and their labeled shelf life was three years from the date of manufacturing[10].

C) SAMPLE IDENTIFICATION

After purchasing, tablets of all the brands were coded as A, B, C, D, and E for paracetamol tablets of different manufacturers. Finally, the coded samples were separated as the same manufacturer and taken for evaluation[10].

TABLE 2. The Required Analysis Tests Used to Evaluate Quality of Brands

TYPE OF TESTS	KEY INFORMATION THAT PROVIDES BY THE TEST
Weight Variation test	Shows the average weight
Disintegration Test	Tells about the time taken by the tablet to disintegrate
Friability Test	Shows how much the tablet can with stand attrition
Dissolution Test	To confirm rate of drug release
Hardness Test	It depicts how much the tablet is prone to friability

D) CHEMICALS

TABLE 3: List of Chemicals

SR.NO.	CHEMICALS
1	Potassium di hydrogen phosphate
2	Sodium hydroxide
3	Distilled water
4	Ethanol
5	Hydrochloric acid
6	Di sodium hydrogen phosphate

E) Equipments

TABLE 4: List of Instrument

SR.NO	INSTRUMENTS NAME
1	Hardness Tester
2	Friability Tester
3	Dissolution Test Apparatus
4	Disintegration Test Apparatus
5	Digital Balance

F) PROCEDURE OF EVALUATION-

Various analytical methods and tests are important for the development and manufacture of pharmaceutical formulations. For the evaluation, The following quality control tests were performed for the tablet brands in the study[10].

METHODS-

1 WEIGHT VARIATION TEST[11]

Materials

Electronic analytical balance, and Tablets.

Method

Twenty tablets of each brand were taken and weighed separately using the electronic balance. To get the standard weight of each tablet, the average weight of all the tablets was computed. To ascertain whether or not each tablet's weight falls within the range, each tablet was weighed separately, and the % weight variation was computed. If no more than two tablets deviate from the percentage restriction and if no tablet differs by more than twice the percentage limit, the tablets pass the USP/BP test.

$$\%\ \text{of weight variations} = \frac{\text{Average weight} - \text{individual weight}}{\text{Average weight}} \times 100$$

2 HARDNESS TEST[11]

Materials

Hardness tester, and Tablets.

Method

From each batch, ten pills were extracted. Tablets were put between the hardness tester's jaws one at a time, and the crushing value was noted. Each tablet's hardness value was assessed, and the average value was computed and contrasted. The Newton (N) unit was used to report the average hardness values.

3 DISINTEGRATION TEST[12]

Materials

Disintegration tester, Distilled Water, and Tablets

Method

The disintegration test measures the amount of time needed to break the tablet and pass all of the particles from mesh size 10 since disintegration is the process of breaking the tablet into minute granules and is a step before drug dissolution, making it a component of the in vitro-in vivo correlation. For this, a USP disintegration device with six glass tubes (Electrolab ED-2L) was utilized. The disintegration test was conducted as part of the USP, and one paracetamol tablet was put in each tube to measure the disintegration time. The basket rack was then placed in a 1L beaker filled with distilled water at 37±2°C. A motor-driven device with a frequency of 28–32 cycles per minute was used to operate the instrument.This technique was repeated for each of the other four distinct brands of paracetamol pills. The disintegration time was recorded after all of the particles from all six tubes moved from the tube mesh to the outer beaker. It was then recorded how long it took on average. The maximum disintegration time for the uncoated tablet is fifteen minutes.

4 DISSOLUTION TEST[13]

Materials

Dissolution tester, Distilled Water, Chemical and Tablets

Method

To find out how much drug content is released after a given amount of time, a dissolution test is conducted. Each brand's tablet dissolution was assessed using a paddle-style device at 50 rpm and 900 ml of pH 5.8 phosphate buffer solution kept at 37±0.5°C. Following a 45-minute period, 10 ml of the sample is removed from the apparatus, filtered, and diluted with 0.1 N sodium hydroxide solution. The absorbance at 257 nm is measured, A1 is 0.715, and the percentage of medication released is computed.

5 FRIABILITY TEST[14]

Materials

Friability tester, and Tablets

Method

Before testing, ten tablets from each brand were chosen, well cleaned, and weighed. After that, the tablets were put into the friability tester's drum and turned for four minutes at a speed of 25 rpm. Tablets were reweighed following 100 revolutions and dedusting, and the following formula was used to determine the friability percentage

$$\% \text{ Friability} = \frac{\text{weight before test} - \text{weight after test}}{\text{weight before test}} \times 100$$

6 ASSAY TEST[15]

Materials

Chemical, Distilled Water, and Tablets

Method

Weigh and grind twenty pills. A precise weight of the powder with roughly 0.15g of paracetamol should be measured. Then, add 50 ml of 0.1 M sodium hydroxide, dilute with 100 ml of water, shake for 15 minutes, and add enough water to make 200 ml. Combine, strain, and dilute 10 milliliters of the filtrate with 100 milliliters of water. Add 10 milliliters of 0.1M sodium hydroxide to 10 milliliters of the resultant solution, dilute with 100 milliliters of water, and stir. At around 257 nm, measure the resultant solution's absorbance at its highest. Determine the amount of paracetamol by using the specific absorbance at 257 nm, which is 715

Result and Discussion-

•**Weight variation:** According to IP/BP, tablets containing 250 mg or more have a weight variation restriction of ±5%. All four brands of paracetamol tablets in this investigation had weight variations that were within ±5% of their average weight.

•**Hardness test:** Friability and disintegration time are always influenced by hardness. The hardness results of every brand of paracetamol in this investigation were deemed adequate.

•**Friability test:** According to IP/BP, the limit of friability is not greater than 1%. We discovered in this investigation that less than 1% of the pills of various paracetamol brands were friable.

•**Disintegration:** IP states that an uncoated tablet will dissolve in 15 minutes. Within fifteen minutes, every tablet of the various brands of paracetamol in this research entirely decomposed.

•**Dissolution:** The IP states that the drug's percentage release is at least 85%, and our investigation revealed that the percentage release for all brands of paracetamol was higher than 85%. The outcome was satisfactory.

•**Assay:**According to the BP the concentration of paracetamol is accepted if it is within the range of 90-110 %. The assay test result for all different brands of paracetamol were found between in range 90 to 100 %.

Table 5.Weight variation, hardness, friability, disintegration, % release of paracetamol, assay of paracetamol tablets

Brand(Cost in Rs.)	Mean Weight in gm ±SD	Hardness in kg/cm2	Friability %	Disintegration time in minutes	% release of Paracetamol at 30 minutes	Assay %
PARACETAMOL	1.08±0.009	174.40 ±27.74	0.50	7.55	81.35%	95.04%
DOLO	0.598±0.003	12.28±0.25	0.27	7.15	87.45%	98.56%
PARACIP	0.593±0.003	7.86±0.41	0.51	5.22	89.56%	99.45%
CALPOL	0.642±0.002	8.34±0.34	0.34	7.38	90.04%	99.76%

ASMOL	0.545±0.001	7.06±0.29	0.44	4.55	90.32%	98.65%

CONCLUSION

The different commercial brands of paracetamol used in the current study all displayed all the parameters under investigation within the designated range, indicating that they are pharmacologically identical, according to theresults of the current study. Therefore, based on its price and shelf-life fluctuation, one brand can be used as a stand-in for another. Additionally, We found that the brand paracetamol had lowest price and that its assessment criteria were reported within a certain range; as a result, it can be chosen as the most affordable medication that a doctor prescribes.

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