COMPARATIVE IN- VITRO STUDY OF GENERIC VERSUS BRAND PARACETAMOL PRODUCTS

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Abstract: *The use of brand-name versus generic drugs remains a contentious issue. The negative effects of non-equivalence result from either too little or too much drug reaching the patient, resulting in either treatment failure or adverse drug reactions. On the other hand, if physicians prescribe higher-priced original drugs to their patients instead of therapeutically equivalent lower-cost generic drugs, the patients must bear the additional cost. The purpose of this study was to compare the bioavailability of paracetamol in a generic versus branded formulation. The purpose of this study was to compare the bioavailability and pharmacokinetic behaviour of two branded formulations of aceclofenac. Weight variation, hardness, friability, disintegration, and dissolution were all tested for compliance with the United States Pharmacopoeia (USP) standards.*

Keywords: *Acetaminophen, Quality Control, Comparative Analysis, Dissolution, Disintegration, Paracetamol, Different Brands Of Paracetamol.*

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INTRODUCTION

Acetaminophen, also known as paracetamol, is a common analgesic and antipyretic drug used to treat fever, headaches, and other minor aches. It is a highly recommended medication for a variety of flu, cold, and body aches. It is a very useful and safe drug for living beings in sufficient quantities, but deliberate or accidental overdose is common due to its widespread availability.It is also a common analgesic compound that is combined with centrally acting compounds such as caffeine, codeine, and dextropropoxyphene, as well as oral decongestants, in a variety of formulations to relieve the symptoms of the common cold, influenza, and sinusitis. Aside from treating headaches and minor aches and pains, it is also used in conjunction with opioid analgesics to treat severe pains such as episiotomy pain, post-surgical pain, and cancer pain. Both acetaminophen and paracetamol are thought to be derived from their chemical names, N-acetyl-para-aminophenol and para-acetyl-aminophenol, respectively.Paracetamol is now a widely used antipyretic and analgesic around the world. Paracetamol is a drug classified as an aniline analgesic derived from coal tar. Phenacetin metabolites produce paracetamol. Paracetamol has been used to replace phenacetin and its combination because it is a highly effective analgesic and antipyretic with fewer side effects and is non carcinogenic at the recommended dose. Even though paracetamol is considered a safe drug, an overdose can cause liver toxicity and renal failure. According to some researchers, paracetamol may alter the lipid profile by increasing triglycerides and total cholesterol while decreasing high-density lipoprotein. Several studies are being conducted by researchers to determine the relationship between paracetamol and cancer. [1- 2]

The World Health Organization (WHO) promotes the evaluation of healthcare expenditure and the improvement of medicine access through the timely evaluation of drug dosage forms to ensure that all medications are pharmaceutically qualified and therapeutically equivalent before reaching the patient.

Despite the fact that many generic drug brands are widely available on the market, effective quality control and monitoring approaches may be insufficient or even non-existent in many developing countries. Concurrently, the introduction of a wide range of generic products has contributed to the widespread distribution of substandard and counterfeit pharmaceutical products in the pharmaceutical market.According to the WHO, substandard drug products are genuine drugs produced by certain authorised manufacturers that do not meet the quality specifications imposed by national or international standards. Around 10% of medical products are found to be falsified or of poor quality, which could be attributed to poor storage conditions, difficulties in medicine access by healthcare providers or patients, technical hindrance and limitations in manufacturing, or weak local authority governance over pharmaceutical product regulations. [3-5]

N-acetyl-para- aminophenol or N-(4-hydroxyphenyl) ethanamide and N-(4-hydroxyphenyl) acetamide are the chemical names for acetaminophen (USA) and paracetamol (Europe). It is an over-the-counter (OTC) medication with antipyretic and mild analgesic properties. The medication inhibits prostaglandin synthesis in the central nervous system and is highly selective for cyclooxygenase enzymes. [6-7]

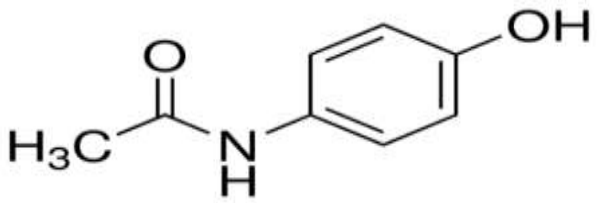

Figure 1: Chemical structure of acetaminophen (paracetamol).

It is also available in a variety of strengths in syrup, solution, suspension, and granule dosage forms. According to the current BCS criteria, acetaminophen is a BCS class 3 compound due to its high solubility and low permeability. Differences in composition rarely affect the extent of absorption of this class of compounds. [8]

Weight variation

Weight variation is a test that estimates the efficacy and persistency of dosage units during manufacturing; any deviation in weight variation is thought to affect the active ingredient of the product. According to official guidelines, a 10% difference was taken for tablets of 80 mg or less, 7.5% for tablets of 80-250 mg, and 5% for tablets greater than 250 mg. The product passed the limit test, and there were no more than two tablets out of the 20 that were outside the official percentage limit, and none of the tablets varied the official percentage limit by more than twice. [9]

Friability

20 tablets were chosen at random, weighed, and placed in a friabilator chamber (Roche Friabilator, Germany) set to 25 rpm for 4 minutes. The tablets were then weighed again, and the weight differences were calculated as percentage friability. The same procedure was followed for all brands of acetaminophen tablets. If the percentage friability is less than 1.0%, the requirements are met. [10]

Disintegration

The term "disintegration" refers to the effect of liquids on tablets by breaking down the internal bonds. However, no exact correlation exists between disintegration and dissolution. It is assumed that the shorter the disintegration time of tablets, the faster the dissolution rate, and vice versa. Simply put, it provides a rough estimate of the bioavailability of dosage units. As a result, it is critical to break down the tablets within the specified time limits of 15 minutes for uncoated tablets and 30 minutes for most coated tablets. [11]

Dissolution

Dissolution is a method for measuring the rate of drug release from solid dosage forms. It also provides information on drug bioavailability by correlating the drug dissolving pattern in the gastrointestinal track prior to reaching the systemic circulation. According to IP, the first dissolution medium was phosphate buffer with a pH of 5.8. The apparatus was filled with 900 mL of buffer and run at (37 0.5) °C for 30 minutes at a speed of 50 r/min with a paddle (apparatus 1). The absorbance was measured in a UV spectrophotometer at 243 nm after a second dilution with the same buffer solution. [12]

Assay: It is critical to set an unbiased concentration of active pharmaceutical ingredient in each batch of medicament to their label claim in order to quantitatively measure the presence, amount, or functional activity of a target entity. Twenty tablets were randomly selected and ground into very fine powder using a pestle and mortar, and the weight of the powder was equal to the standard one. The weights of the standard and samples were calculated using the final solution concentration for the UV spectrophotometer.

Objectives

1. To compare the bioavailability of Paracetamol in generic versus brand product
2. To evaluate the IPQC tests between tablets of different brands.
3. To study of Different brands of paracetamol tablets determining different parameters like weight variation, hardness, friability, disintegration time, dissolution.
4. To evaluation of formulation various analytical methods according to USP and BP standards evaluation.

REVIEW OF LITERATURE

Paracetamol is the most commonly used analgesic/antipyretic agent for treating mild to moderate pain. It is quickly absorbed and has a half-life of about 2 hours (Dougall et al., 1983; Nimmo and Prescott, 1978). Serum concentrations between 10 and 20 g mL-1 are generally considered therapeutically effective, whereas serum concentrations greater than 150 g mL-1 may cause hepatic necrosis (Winek, 1976). [13]

The formulation of paracetamol affected its pharmacokinetics in humans (Steinigen, 1988; Degen and Maier, 1984; Haile et al., 1992; El-Sousi et al., 2002). The current study compares the relative bioavailability of two generic paracetamol tablet formulations (Decamol and Otamol) to the innovator's brand (Dexamol). The bioequivalence of two locally manufactured tablet brands was evaluated in comparison to an imported tablet brand. Data was collected both in vivo and in vitro.In vivo data included saliva concentrations from ten volunteers. The use of saliva concentration data for paracetamol bioavailability assessment was deemed feasible due to the ease of collecting and analysing saliva samples, as well as the good correlation between saliva and plasma concentrations of paracetamol (Cardot et al., 1985). In the current study, free paracetamol in saliva was measured using a simple and sensitive colorimetric method (Price et al., 1983). [14-16]

RESEARCH METHODOLOGY

To carry out this experiment, various official books such as USP and BP were used to determine the in vitro quality tests using various procedures and analytical tests. During the evaluation of various brands of paracetamol tablets, we determined various parameters such as weight variation, friability, hardness, drug content, identification test, disintegration time, and dissolution profile. We discovered that different brands have acceptable value by performing weight variation and friability tests.

Books, educational and development journals, government papers, and print and online reference resources were among the secondary sources we used to learn about the composition, use, and consequences of Comparative Bioavailability studies of paracetamol brands in humans.

RESULT AND DISCUSSION

Continuous in-vitro testing of pharmaceutical dosage forms is critical for ensuring optimal quality control and is required for bioequivalence studies. Five different acetaminophen tablet brands were evaluated for weight variation, hardness, friability, disintegration, and dissolution.

Table 1: Observation for weight variation of different brands. (mg)

No.	Brand	Average weight	Upper limit	Lower limit
1	Np-1	595.915	612.800	583.800
2	Np-2	570.000	589.300	548.100
3	Np-3	595.625	620.900	572.700
4	Np-4	571.055	581.000	564.600
5	Np-5	576.490	583.300	568.400

Weight variation

According to the BP and IP specifications, all tablets of each brand passed the weight variation test with less than 5% deviation for tablets containing more than 250 mg. Table 1 [17]

At the time of the investigation, all drug samples had reached the end of their shelf life. Table 2 displays the characteristics of the brands under consideration. FDA recommends that 1 values less than 15 and 2 values greater than 50 ensure equivalence between dissolution curves and indicate an average difference of no more than 10% at each sample time point.

Table 2: Pair-Wise Comparison of Dissolution Profiles for 500-mg Acetaminophen Tablet Formulations

Brand Code	AUC (min %)	MDT (min)	DE (%)	f_2	f_1
A	10502.0	16.4	87.5	N/A	N/A
B	9758.0*	14.5	81.3*	67	4
C	9775.5*	14.5	81.4*	53	12
D	10337.5	12.8	86.1	61	10
E	11438.5*	9.9*	95.3*	48.25	17

With this requirement in mind, the dissolution curves for brands B, C, and D (but not E) were similar and thus considered pharmaceutically comparable to that of the reference formulation, ensuring their interchangeability. Table 2 [18]

The dissolution of a drug from an oral solid dosage form is a necessary criterion for its bioavailability, and as such, the drug must be solubilized in the gastrointestinal tract's aqueous environment in order to be absorbed. Figure 2 shows that all tested brands met the USP requirement of releasing no less than 80% of the drug after 30 minutes. [19]

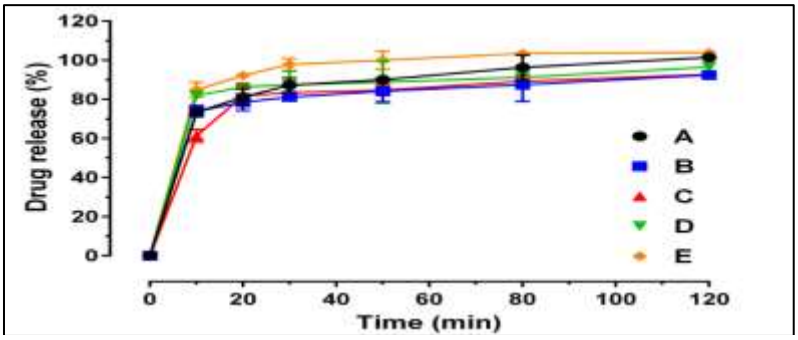

Figure 2: Dissolution profiles of commercially available acetaminophen 500-mg tablet brands

The purpose of this study was to look at the physicochemical properties of locally and multinationally available paracetamol tablets. All 500 mg (uncoated) paracetamol tablet brands were compared in terms of physical and chemical parameters.

CONCLUSION

Although physicochemical tests such as weight variation, friability, disintegration, dissolution, and assay were detected varying by brand, they were all found to be within defined limits. As an over-the-counter medication, paracetamol consumption is excessive. As a result, it is critical that each brand be genuine, well-manufactured, and well-marketed. As a result, additional research into the quality of paracetamol is required for safe human consumption. We concluded from the results that each branded tablet used for comparative evaluation produces different results than the others, but no one exceeds the limits specified in official books.

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