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Research Article

A Comparative Study of Quality on Conventional Paracetamol Tablets Available in Pakistan

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Abstract:

Background: Paracetamol (Acetaminophen) is used as over the counter (OTC) medicine for relief of pain and fever. Paracetamol is available in different brands in Pakistani pharmaceutical market. **Objective:** To assure the quality control parameters of different brands of paracetamol in Pakistan. **Methodology:** The pharmaceutical and chemical equivalence of five brands of paracetamol were assessed. For ethical concerns, the brands were coded as PRC-1, PRC-2, PRC-3, PRC-4 and PRC-5. Study was conducted in quality control laboratory of Adamjee Pharmaceuticals during December 2015 to February2016. Identification, physical characteristics, thickness, diameter, weight variation, hardness, disintegration time, percent label claim (Assay) and dissolution rate were calculated for each brand using monographs of British Pharmacopeia and United States Pharmacopeia. **Results:** Identification, physical characteristics, thickness, diameter, weight variation, hardness, and disintegration time, percent label claim (Assay), and dissolution ratewere calculated for each brand and the results were within the specifications provided by British Pharmacopeia and United States Pharmacopeia. **Conclusion:** All the brands selected in the study showed results within the limits assuring quality standards of manufacturing.

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INTRODUCTION:

Oral dosage form is one of the most common method used for the administration of drug, it includes Tablets, Capsules, Suspensions, Solutions and for oral suspensions. Among all, tablets and capsules dominate the other dosage forms. Even tablets are more widely used over capsules being tempered free, cost effective, and stable. History of tablet is old to 150 years back when it was compressed for the first time by Thomas Brokedon, since that time researchers had made contributions to meet the stability of dosage form from batch to batch. Pharmaceutical Industries have to produce tablets that are strong enough (low Friability) as to meet the environmental conditions[11].Manufacturing process and raw materials used in formulation affects the quality of finished product. To ensure that the product is of quality it is necessary to determine the parameters of tablets during manufacturing [5].

Quality of the finished product depends upon the early developmental process[1]. Drugs not meeting the quality criteria may cause serious health complications, may result in drug adverse reactions, may produce drug resistance in the individual, and can increase the risk of morbidity and mortality [3].It is the responsibility of drug regulatory authority of the country to ensure the quality of drug [12].A drug molecule once mixed with excipients can be available in tablet form, excipients are used to achieve a tablet dosage form of desired weight, volume, flow and compactness. One of another function of excipient is to control the release of drug from dosage form [13].For a single generic drug, various brands are available. Quality of all available brands needs to be assessed in order to provide an efficacious formulation, this responsibility increases in case of over the counter (OTC) medicines, quality of the product vary from manufacturer to manufacturer[2].

Paracetamol (acetaminophen) chemically N-acetyl-p-aminophenol is easily available, overthe counter medicine used as antipyretic and analgesic drug. Paracetamol is administered by different routes including oral, rectal and intravenous[5]. Paracetamol is effective in cancer pain in combination therapy[6].Paracetamol is safe NSAIDS in patients with peptic ulcer as the molecule has no

antiinflammatory activity and doesnot produce any damage to gastrointestinal layers[14].Paracetamol molecule was first reported in 1893, due to paracetamol induced metheamoglobinemia, the molecule was avoided for 60 years. Later, the toxicity theory was disproven by three separate research groups and the molecule was declared as safe as oral dosage form in 1950's by United States [15].

The distribution of paracetamol in the body fluid is uniform; apparent volume of distribution of paracetamol is 1 to 1.2 L/Lg. Excretion of paracetamol is observed in breast milk as it can cross the placental layer. Plasma protein binding depends upon the concentration of paracetamol, it is negligible at therapeutic concentration, however, as the concentration increases, plasma binding protein increases [4]. Paracetamol is used for analgesia and antipyretics; its antiinflammatory and antirheumatic activities are not sufficient to declare it as drug of choice for inflammation and rheumatic disorders[14].

Materials and methods:

Paracetamol (standard) was gift from Adamjee Pharmaceuticals (Pvt.) Ltd. Pakistan. In the study, five commercially available paracetamol 500 mg tablets with different brands in Pakistan were purchased (randomly selected) from registered pharmacy stores. For ethical concerns, the products were coded as PRC-1, PRC-2, PRC-3, PRC-4 and PRC-5 so that the identity of the manufacturer can be blinded and only researchers may know manufacturer. Below are the details of five randomly selected brands of paracetamol.

Reagents

All the reagents used in the study were of pharmaceutical grade, standard solutionswere prepared using standard operating procedures and calibrated instruments. Potassium dihydrogen orthophosphate (Merck, Germany)was used to prepare phosphate buffer(pH 5.8) solution.Sodium hydroxide (0.1 M) was prepared by dissolving 4.2 gm of sodium hydroxide pallets (BioM Laboratories USA) in 1 liter of de ionized water.

Visual Inspection

All the tablets of selected brands were subjected to visual inspection before start of the research.The shape, size and color of different brands were examined carefully.

Thickness and Diameter Inspection

Ten tablets from each brand were selected for thickness and diameter test.Thickness and diameter were determined by using Vernier caliper.Mean thickness, diameter and their standard deviation (S.D) and percentage relative standard deviation (RSD) were calculated.

Weight variation

Weight variation of ten tablets from each brand was performed. Tablets were weighed individually using analytical balance (TE214S, Sartorious Germany). The average weight, weight variationand standard deviation and percentage relative standard deviation.

Hardness test

Crushing strength of ten randomly selected tablets was determined by using hardness tester (VEEGO, INDIA).

Friability Test

Twenty tablets from each brand were weighed accurately and were subject to rotation in friabilator. The tablets were rotated at 25 rpm. Tablets were weighed after rotation; the friability percentagewas calculated by using the formula

$$\% \text{ Friability} = \frac{W1-W2}{W} X\ 100$$

Where,

W1= Weight of 20 tablets before rotation

W2= Weight of 20 tablets after rotation

Percent Label Claim (Assay)

To calculate the percent label claim of paracetamol in five brands, 20 tablets were selected randomly from each brand and weighed to obtain average weight. Tablets were crushed by motor and pestle after being weighed. Tablets to be crushed until it converts into fine powder form. From average weight calculate and then weigh the powder that is equivalent to 0.15 g of paracetamol. In a 200 ml volumetric flask add 50 ml of 0.1 M sodium hydroxide solution, 100 ml of water and shake well for 15 minutes, make up the volume to 200 ml by adding de-ionized water, mix well and then filter. Pipette out 10 ml of resulting solution, add 10 ml of sodium hydroxide and make up the volume to 100 ml by using de-ionized water.

Standard solution is prepared accordingly. Absorbance of sample and standard were measured at 257 nm using spectrophotometer (UV-1601, SHIMADZU, JAPAN). Solution of 0.1 M sodium hydroxide was used as blank[9].

Disintegration Time

Six randomly selected tablets from each batch were used to determine the disintegration time. For the test, tablets were placed in the frame of baskets at temperature 37 ^{o} C as per condition described by British Pharmacopeia 2013. Disintegration time was calculated using disintegration apparatus (VTD, 3D, VEEGO, INDIA).

In-vitro Dissolution Studies

Dissolution rate was determined for 6 randomly selected tablets using dissolution apparatus paddle II (VEEGO, INDIA). Dissolution medium used was phosphate buffer pH 5.8 (900 ml at 37 ± 0.5 ^{o}C). Rotations of paddles were 50 revolutions per minute. Sample was withdrawn after 45 minutes, 10 ml sample was diluted to 200 ml by using 0.1 M

sodium hydroxide to obtain a solution containing 0.00075% w/v of paracetamol. Standard solution was prepared accordingly. Absorbance was measured at 257 nm with 0.1 M sodium hydroxide in reference cell[9].

Quality Assurance

In the study, British Pharmacopeia 2013 and United States Pharmacopeia 32 National Formulary 27 were followed during determination of physicochemical properties. All the chemicals used in the research were of pharmaceutical grade.

Data Analysis

Data was analyzed using simple statistical analysis. Standard deviation and percentage relative standard deviation were calculated for weight variation, thickness, hardness and diameter.

Results

Visual Inspection

All the tablets of selected brands were meeting the visual inspection criteria. There was no sign of chipping, capping, sticking or picking in the tablets. Literature on the strip was clear and batch number along with expiry was readable. No physical degradation of tablets observed.

Thickness and Diameter

Mean, standard deviation and percent relative standard deviation of selected tablets of five brands are expressed in Table 2.

Weight Variation

Limit for variation is ± 5 % if the tablet weighs 250 mg or more[9]. Table 3 shows mean weight, standard deviation and percent standard deviation of selected brands of Paracetamol.

Hardness

Tablet hardness is of great importance as it is responsible for the disintegration process of tablet in the body fluid, if the hardness is high it will decrease the dissolution profile or tablet will be fragile if the hardness is low. An appropriate hardness is required for tablets. Official compendia's does not provide limit for hardness as it depends upon the formulation. Table 4 shows hardness of all brands of Paracetamol.

Disintegration Time

Disintegration time is calculated to ensure batch to batch product uniformity. Disintegration time for conventional tablets should not be more than 15 minutes [10].Table 5 shows disintegration time of all brands of paracetamol meeting the criteria.

Percent Label Claim (Assay)

Content of paracetamol in paracetamol tablets must be not lower than 95.00 % and must not be more than 105.00 % of the percent label claim (Assay)[9]. Table 6 shows that all the brands meet criteria specified by British Pharmacopeia 2013

***In-vitro* Dissolution**

Release profile of drug is important to calculate the oral bioavailibity of drug. Dissolution of drugs plays vital role in in-vivo and in-vitro correlations [8]. Table7 shows dissolution of all the brands of paracetamol.

Discussion

Paracetamol is widely used over the counter (OTC) medicine. The study made an attempt to access the quality parameters of available paracetamol tablets in Pakistani market. Paracetamol is manufactured and marketed by several Multinational and national pharmaceutical industries. The study compares different physico-chemical parameters of randomized selected brands of paracetamol. All the selected brands showed results within specifications confirming quality of manufacturers.

Although all the quality test plays a vital role in assessing the quality of drug; however, dissolution testing of solid oral dosage form has vital importance [5].

The weight uniformity of five commercially available brands gave values within specifications of United States Pharmacopeia.

Previously study on different paracetamol tablets in India revealed thatnational pharmaceuticalcompanies did not pay much attention to weight variation parameter of the tablet in comparison to Multinational Companies. The study showed weight variation upto 15 % while only 2.5 % by multi nationals [2].

For conventional dosage form friability is one of the important tool to assess the crushing strength of the tablet as tablet must have suitable strength for transportation, packaging and shipping. All the five brands used in the study are conventional dosage form and met USP specifications (friability less than 1%)

Previously a study has been conducted in Ethiopia on quality parameters of marketed paracetamol by legal and illegal manufacturers, the study showed paracetamol manufactured by legal manufacturer met USP specifications while paracetamol of illegal manufacturers fails to comply with the specifications [3].

The results obtained from pharmaceutical analysis of active ingredient of five brands of paracetamol tablets showed values within BP specifications 95% to 105%.

Disintegration time of all the five brands of paracetamol were within the BP specifications (less than 15 Mints). Previously a study has been conducted in Bangladesh showed that disintegration time of paracetamol tablets are satisfactory and was within 5 minutes [6].

Bioavailabilityand absorption of drug is dependent on dissolution. In the present study, the release of paracetamol from all tablets was immediate release; drug release in 45 mints were more than 70% meeting BP Specifications.

Previously a study has been conducted in Egypt on comparison of dissolution profile of paracetamol tablets and revealed that all the tablets complies with BP specifications [4].

Limitations of study

The study design was experimental; there might be chance of systematic error or random error.

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Table No. 1: Shows details of five randomly selected brands of paracetamol

Code	Mfg. Date	Exp. Date	Mode of Packaging
PRC-1	02-2015	02-2020	Blister
PRC-2	05-2015	05-2020	Blister
PRC-3	02-2015	02-2020	Blister
PRC-4	02-2015	02-2018	Blister
PRC-5	03-2015	03-2018	Blister

Tables No. 2: Thickness and diameter of Five Brands

Code	Thickness (Mean)	Standard Deviation (S.D)	Percentage Relative Standard Deviation (R.S.D)	Diameter (Mean)	Standard Deviation (S.D)	Percentage Relative Standard Deviation (R.S.D)
PRC-1	4.572	0.115835	2.53	12.213	0.094757	0.77
PRC-2	4.359	0.148058	3.39	12.395	0.232247	1.87
PRC-3	3.869	0.071095	1.78	12.633	0.112057	0.88
PRC-4	3.88	0.067495	1.73	12.296	0.183012	1.48
PRC-5	4.45	0.05921	1.33	12.10	0.178651	1.47

Table No. 3: Hardness of Five Brands

Code	Hardness in Kg (Mean)	Minimum Hardness in Kg	Maximum Hardness in Kg
PRC-1	9.63	6.8	13
PRC-2	7.82	5	10.2
PRC-3	13.5	10	17
PRC-4	9.77	7	12
PRC-5	6.5	5.5	7.2

Table No. 4: Disintegration Time of Five Brands

Code	Disintegration Time	United State Pharmacopeia Specification	Remarks
PRC-1	04 Minutes 13 Seconds	Not More Than 15 Minutes	Complies
PRC-2	50 Seconds	Not More Than 15 Minutes	Complies
PRC-3	04 Minutes 10 Seconds	Not More Than 15 Minutes	Complies
PRC-4	01 Minute 10 Seconds	Not More Than 15 Minutes	Complies
PRC-5	04 Minute 15 Seconds	Not More Than 15 Minutes	Complies

Table No. 5: Percent Label Claim of Five Brands

Code	Percent label claim	British Pharmacopeia Specifications	Remarks
PRC-1	99.90 %	95.00 – 105.00 %	COMPLIES
PRC-2	98.76 %	95.00 – 105.00 %	COMPLIES
PRC-3	98.25 %	95.00 – 105.00 %	COMPLIES
PRC-4	98.68 %	95.00 – 105.00 %	COMPLIES
PRC-5	99.83 %	95.00 – 105.00 %	COMPLIES

Table No. 6: Single Point Dissolution Study if Five Brands (at 45 Minutes)

Code	Time of sample	Average drug release	British Pharmacopeia Specification	Remarks
PRC-1	45 Minutes	98.90 %	Not Less Than 70 %	Complies
PRC-2	45 Minutes	97.20 %	Not Less Than 70 %	Complies
PRC-3	45 Minutes	96.20 %	Not Less Than 70 %	Complies
PRC-4	45 Minutes	97.60 %	Not Less Than 70 %	Complies
PRC-5	45 Minutes	91.40 %	Not Less Than 70 %	Complies

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