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Post-Market *In-Vitro* Comparative Evaluation of Quality Control Parameters of Paracetamol Compressed Tablets Manufactured in Local Industrial Zones of Kpk Pakistan.

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Paracetamol (acetaminophen) is an OTC drug available also in dosage form of compressed tablets in almost all countries, being extensively used as antipyretic and general analgesic. In KPK Pakistan numbers of brands are available manufactured in local industrial zones. Here in this laboratory research we have tried to follow the simple approaches i.e. the British Pharmacopoeia and USP and other standard book's standards and procedures to evaluate the quality parameters of different brands (3 brands A, B and C), by selecting samples of different batches (3 batches of each), manufactured in industrial zones of KPK Pakistan (by 3 different manufacturers). Types of quality tests performed are weight variation, disintegration time, dissolution, hardness and friability. Finally the results evaluate no significant deviations from the compendial standards and specifications, and we got the aim of our study that these brands of local manufacturers in KPK are safe enough and could be used to achieve the desired therapeutic effect which has been discussed in paper.

Keyword: Post Market Quality Control Parameters, Compressed Paracetamol Tablets, Weight Variations, Disintegration Time, Dissolution, Hardness, Friability.

1. Introduction

It has been estimated that at least 90% of drugs that have been intended to produce systemic effect are administered by the oral route[1]. So this fact extensively highlighting the importance of tablets as a dosage forms.

Compressed tablets or standard compressed tablets refer to standard uncoated tablets made by compression. Drugs compressed in such tablets are usually intended for systemic effect and have some aqueous solubility, the drug disintegrate from the tablet in GI contents and disaggregation of granular particles occurs which then leads to dissolution of particles in GI fluids and ultimately leads to absorption[2].

Post market qualitative studies and evaluations include activities performed to get more precise information of a product being get marketing authorization and availability for community use. The data (qualitative and quantitative) obtained as a result of such post market evaluation could be used for product development and improvements in product quality as per standards. As it is known that the market authorization of a product for community use is granted by regulatory authorities on behalf of limited data obtained by

clinical trials and scientific literature, so the post market evaluations and as a result obtained data could be extensively used to judge the approved products for their quality, efficacy and safety for general end consumers. So post market qualitative evaluation should be a continuous activity throughout the product life cycle. Post market evaluation of a product has been identified to include: evaluation and investigation of reported product complaints and procedure for production and review of label claim; general public access to data taken and reported to drug regulatory authorities, and in vitro testing of product for complaints to official specifications[3]. The therapeutic effectiveness of a compressed tablet relay on minimum of two factors, i.e. content uniformity (the actual label claim) and its adequate bioavailability. The main aim of an oral compressed tablet is to make available the drug to human body at a specific and defined quantity through GIT in order to gain a therapeutic outcome; so the formulation of a product have a direct effect on the quality parameters: such as weight variation, disintegration, dissolution, hardness and friability[4]. Also the physiochemical properties of excipients and API are also important and at the same time the processes of manufacturing[5,6]. Moreover, in order to maintain a qualitative consistency in batch to batch production quality control parameters are significant tools to be considered and should be performed for every product. All quality control parameters are inter related and have effect on drug absorption, availability to body etc[7].

1.2 Paracetamol and its chemistry

Paracetamol or acetaminophen is active metabolite of phenacitin (see fig -1). Paracetamol is extensively used OTC drug; chemically paracetamol is 4-hydroxy acetanilide[8]. Paracetamol a non-opioid analgesic is indicated for headache, transient musculoskeletal pain, and as anti pyretic. Paracetamol has no demonstrable anti inflammatory activity; if over dosed causes may causes hepatic damage[9].

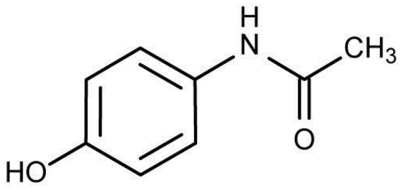

Fig 1:paracetamol chemical structure

IUPAC Name: N-(4-hydroxy phenyl) acetamide.
Chemical formula: C8H9NO2
Molecular weight: 151.17

Other properties:

Physical status: white crystalline powder
Melting point: 168-172'C
Solubility in water: sparingly soluble
P^H: 5.5-6.5
Stability: Stable in normal conditions. [10]

Objective

The objective of the study was to evaluate the comparative quality parameters between the tablets of three brands manufactured and available in KPK Pakistan, because standard quality parameters are essential for standard quality products.

2. Materials and Methods

Materials:

Total three commercially registered brands of paracetamol tablets were used in the study. Two brands taken of the local manufacturer of hayatabad industrial estate Peshawar KPK Pakistan, and one brand taken of a local manufacturer of Haripur industrial zone haripur KPK Pakistan, all brands were purchased from the retail pharmacies in KPK. USP and British pharmacopoeia were used as standard for the evaluation study.

- For dissolution testing instrument used: dissolution apparatus II i.e. paddle apparatus DL-0708-CURIO.
- UV-Spectrophotometer: model UV-1800 240V, CAT NO. 206-25400-38, Serial no. A11454600909CA 220-240V, Approx 50-60Hz-Shimadzu corporation Kyoto Japan.

- For hardness: strong cobs hardness tester HT-0607-CURIO.
- For friability: Roche Friabilator FB-0607-CURIO.
- A disintegration tester i.e Eagle scientific limited, Nottingham.
- Analytical balance (ADAM AFP 110L,india).

2.3 Methods:

- **Determination of weight variation**
  Twenty tablets from each three brands of paracetamol were weighted individually with the mentioned analytical balance and average weight and the percent deviation was determined for each brand.
- **Determination of hardness**
  For determination of hardness 20 tablets were selected randomly from each brand and are determined by using the mentioned hardness tester.
- **Determination of friability**
  Ten tablets from each brand were selected randomly, de dusted and weighted using analytical balance, then subject to Roche Friabilator for 100 revolutions, then again de dusted and friability is calculated as:

$$\%\text{age friability} = \frac{\text{difference in weight}}{\text{Total original weight}} \times 100$$

- **Determination of disintegration time**
  Disintegration time was determined by taking six tablets randomly from each brand in 900m beaker filled with water at 37'C using disintegration apparatus mentioned above.
- **Dissolution tests**
  The adequate availability of drugs to the body fluids is a significant pre requisite for any product intended to be taken orally-to be systemically effective. Dissolution is the rate of mass transfer from the product to the bulk of solution[11].
  The dissolution tests were conducted using BP apparatus II (paddle apparatus) in six replicates for each selected brand. The medium used was phosphate buffer (900ml at 37'C+-0.5'C for each replicate) of pH 5.8+-0.05; RPM for tests was 50. Withdrawn a sample of 20ml of the medium at various time intervals i.e. 10, 20,30,45,60 minutes, filtered it and diluted with 0.1M NAOH and absorbance was measured at 257nm. The total contents of paracetamol in each sample were calculated by taken 715 as the value of A (1%, 1cm) at maximum at 257nm[12].

3. Results and Discussion

This in vitro comparative evaluation study has been conducted on three different brands (naming A, B, C) of paracetamol conventional release compressed tablets, manufactured and available in KPK Pakistan; and standard books and procedures were being used for this work specially BP and USP.

The selected brands are:

Table-1: samples of paracetamol tablets

Code	Brand name	Dosage form
A	Aksopol	Compressed tablets 500mg
B	Pedrol	Compressed tablets 500mg
C	parasol	Compressed tablets 500mg

3.1 Other results are summarized in given below tables:

Table-2: hardness and friability tests results

Product	Hardness kg/cm^2	Percent Friability
A	11.3	0.82
B	7.8	0.47
C	16.6	1.0

Table-3: summary of the test results of weight variation DT.

Product	Weight variation test limit (mg)	Average disintegration time (min.sec)
A	576	7.50
B	586.7	9.23
C	573.2	15

Table-4: summary of the test results of dissolution

Time interval (minutes)	Percentage release of paracetamol contents		
	A	B	C
10	82.5	77.3	61.8
20	94.4	85.4	69
30	95.2	87.2	76
45	96.4	91.9	91.2
60	99.7	95.2	95.6

- **Weight variation**
  Weight variation test is being conducting for the tablets having weight more than 325mg; and shows the relative variations of active ingredient and excipients.
  In this work, all brands were considered not to deviate more than 10% of the average weight and there should not be more than 2 tablets deviating from average by more than 5%. All brands comply BP specifications and no brand deviate by 5% of the average weight. Weight variation gives a rough idea of content uniformity, but not a confirmatory test.
- **Hardness**
  Hardness is the amount of strength or resistance to withstand mechanical shocks. As we know that hardness is not an official test so there is no such a compendial limit for hardness but a force of about 4kg is considered minimum requirement for a satisfactory tablets [13]. Hardness also influence friability and disintegration, i.e. the less hard a tablet, the more friable and less time it takes to disintegrate. All the brands were being found satisfactory to standard of hardness except brand C.
- **Friability**
  Friability test evaluate the tablet strength to withstand coating, packaging and shipping and other manufacturing processes. According to BP specifications, the total weight loss should not exceed one percent and no tablet shows any type of breakage or crack. [14]
- **Disintegraton**
  As the disintegration time for conventional tablets is within 15 minutes, and in this study the paracetamol tablets are conventional tablets; so all brands here comply the BP specifications of disintegration test. Disintegration could be related to dissolution and similarly availability of drug to body (absorption) (**FDA 2009**), and finally the therapeutic efficacy of product.
- **Dissolution**
  According to BP not less than 70% of the claim amount of the drug should release from product in 30 minutes. Product A releasd 95.2%, B 87.2% and C 76% of drug; so results satisfied BP specifications.

Uniformity of weight, disintegration and dissolution are considered official tests and friability and hardness non official tests.

4. Conclusion

As a result of this study, we have concluded that only minor deviations in some aspects have been seen, e.g. brand C hardness, and slow dissolution rate, and all the brands comply the compendial standards, and the brands of various

manufacturers in KPK are not significantly different.

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