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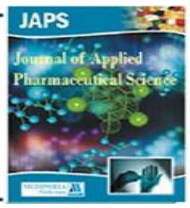

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A comparative study of physical parameters of selected ketorolac tromethamine tablets available in the pharma market of Bangladesh

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ABSTRACT

Quality of pharmaceutical product is very important because drugs must be marketed as safe and therapeutically active formulations whose performance is consistent and predictable. The evaluation of the physical characteristics of the pharmaceutical products can ensure their quality as well as bioavailability and impart optimum therapeutic activity. Ketorolac tromethamine was chosen for this comparative study because this drug is widely used worldwide for treating moderate to severe pain. The present study compared the weight variation, hardness and the abrasion withstanding ability of eight brands of Ketorolac tromethamine tablets marketed in Bangladesh following USP guidelines. All eight brands of Ketorolac tromethamine tested conformed to the USP weight variation test. All the brands had average hardness of ≥3 kg which was satisfactory for immediate release tablet like ketorolac tromethamine. All the brands had shown their friability variation within ±1% range specified by USP. Standard deviation was calculated among all the brands which was very close to individual percentage friability of all the brands. All the brands of ketorolac tromethamine complied with USP requirements of physical quality parameters. It follows that these brands will show good disintegration and dissolution profile which would further help in achieving optimum bioavailability and in fulfilling the patient demands.

Keywords: *Ketorolac tromethamine*, weight variation, hardness, friability, USP.

INTRODUCTION

Quality is the collection of features and characteristics of a product that contribute to its ability to meet given requirements and also in creating standards for producing acceptable products (Marx, 2010). Quality can be defined as the measurement of excellence or state of being free from defects, deficiencies, and significant variations. ISO 8402-1986 standard defines quality as "the totality of features and characteristics of a product or service that bears its ability to satisfy stated or implicated needs (Luthra, 2007). Quality is measured by the degree of conformance to predetermined specifications and standards, and deviations from these standards can lead to poor quality and low reliability. In a pharmaceutical sense, quality means checking and directing the degree or grade of excellence of processes and products. To the ethical pharmaceutical manufacturer it implies a detail system of inspection and control covering the production, evaluation, distribution of every drug bearing the company's label. It is the purpose of these operations to produce medication of superior efficacy, safety and elegance and to provide assurance to physician, pharmacist and the consumer that given product performs uniformly and in a manner satisfactory for the purpose for which it is recommended (Levi and Walker, 2010).

The poor quality of drugs has been linked to counterfeiting of medicines, chemical instability especially in tropical climates, and poor quality control during manufacture (WHO, 2010). Quality of a pharmaceutical product can be assured by evaluating different physical characteristics of the product such as weight variation test, hardness test, friability test etc. as well as disintigration, dissolution and assay tests following standard methods given by different drug control authorities like USP, BP etc. Evaluation of the physical characteristics can ensure the quality of drug and thereby impart optimum therapeutic activity as well as bioavailability (WHO, 2010).

If a number of different formulations are available for the same active ingredient, it is essential to ensure that all of them are pharmaceutically equivalent. Pharmaceutical equivalence is the condition in which drug products, containing the identical quantity of active substance (but not necessarily containing the same excipients), in an identical comparable dosage form, meets all applicable standards of identical strength, quality, purity and potency (Apurba *et al*., 2011).

Ketorolac tromethamine is a highly potent member of a new class of analgesic and anti-inflammatory agents. (Rooks *et al*., 1985). Ketorolac is indicated for short-term management of moderate to severe pain (American Society of Health-System Pharmacists, 2011). For effective control of pain associated with seasonal allergies and other disease, it is very important that the product quality is maintained throughout and to ensure that different physical parameters as well as other quality control parameters are evaluated. The FDA has approved an intranasal formulation of ketorolac tromethamine (Sprix Nasal Spray) for short-term management of moderate to moderately severe pain requiring analgesia at the opioid level (MHRA, 2007).

The present study was aimed to evaluate the brands of Ketoroalc tromethamine tablet available in Bangladeshi pharma market with respect to weight variation, hardness and the abrasion withstanding ability of tablets.

MATERIAL AND METHODS

Sample collection and brand selection

There are approximately thirty seven brands of ketorolac tromethamine in the pharma market of Bangladesh (According to QUIMP, a book containing all the names of drugs available in pharma market of Bangladesh). Among them eight available brands were selected for the study of physical parameters. All the brands were labeled as KT. They were given the number from one up to eight for the convenience of study.

Weight Variation Test

For each brand, ten tablets were randomly selected and weighed individually with the help of an analytical balance (ELB 3000, Shimadzu, Japan). The average weights were determined and the percentage deviations from mean values were calculated. (USP, 2007). The percentage weight variation for each tablet was estimated according to the following formula:

% Weight variation = (Average weight-Individual Weight) / Individual Weight × 100

Hardness Test

The hardness of 10 tablets was determined for all the brands, using “Monsanto” type hardness tester (Intech, Korea). (USPh, 2007). The mean crushing strengths (hardness values) were determined.

Friability Test

For friability test, twenty tablets were randomly selected, weighed and placed into the friabilator (Veego, Germany) chamber set at 100 rpm for 1 minute. The tablets were weighed again and the differences in weight were calculated as the percentage friability (table 1). The same was done for all the selected brands. (USP, 2007). The percentage losses of 10 tablets were calculated as per following equation:

% Loss = (Initial weight-Final weight) /Initial weight ×100

RESULT AND DISCUSSION

Weight Variation Test

The objective of the weight variation test is to ensure - good manufacturing practices (GMP), appropriate size of the tablets and the content uniformity of the formulation (Yoshida, 1999). The United States Pharmacopoeia (USP) provides criteria for tablet weight variation of intact dosage units. All the brands complied with the compendial specification for uniformity of weight which states that tablets weighing 130 mg or less, weights of not more than 2 tablets should not differ from the average weight by more than 10% and none deviates by more than twice that percentage (Lachman, 1986).

All eight brands of Ketorolac tromethamine tested conform to the USP weight variation test showing a standard deviation <6 (Table 1).

Table 1: Weight variation of eight brands of Ketorolac Tromethamine.

Sample ID	Average weight (mg) ±SD	Range (%) weight variation (n = 10)
KT1	138.04±1.99	-3.59 to +2.41
KT2	187.61±1.49	-2.12 to +2.29
KT3	158.84±3.42	-4.38 to +6.38
KT4	166.00±1.26	-2.04 to +1.74
KT5	186.74±0.50	-0.51 to +0.82
KT6	186.06±2.12	-3.09 to +3.25
KT7	105.73±2.12	-3.75 to +2.39
KT8	129.65±1.00	-2.27 to +1.13

Hardness Test

Tablet hardness has been defined as the force required for breaking a tablet in a diametric compression test. Hardness tests helps to measure whether a tablet inherits adequate hardness to withstand consumer handling, at the same time must provide satisfactory disintegration and dissolution results. If the tablet is too hard, it may not disintegrate in the required period of time to

meet the dissolution specifications. Again, if it is too soft, it may not be able to withstand the handling during subsequent processing such as coating or packaging and shipping operations.

In the present study, all the brands of ketorolac tromethamine showed the standard deviation within the compendial range. Among the 8 brands of Ketorolac Tromethamine tested, KT4 and KT8 showed comparatively higher hardness (4.85 and 4.15 kg, respectively) than other brands (Table 2).

Table 2: Hardness of eight brands of Ketorolac Tromethamine.

Sample ID	Average Hardness (kg) ±SD	Average Hardness (N) ±SD
KT1	2.65±0.34	25.99±3.31
KT2	3.1±0.32	30.40±3.10
KT3	3.85±0.24	37.76±2.37
KT4	4.85±0.24	47.56±2.37
KT5	3.65±0.53	35.79±5.19
KT6	3.95±0.28	38.74±2.78
KT7	3.5±0.33	34.32±3.27
KT8	4.15±0.24	40.70±2.37

Friability Test

The United State Pharmacopoeia states that the friability value of tablets should be less than 1% (USP, 2007) and as such all the brands of ketorolac tromethamine tablets had passed this friability specification (Table 3).

Table 3: Friability Test of eight brands of Ketorolac Tromethamine.

Sample ID	Initial weight of tablet (gm)	Final weight of tablet (gm)	Percentage of Friability	Average percentage friability	Standard Deviation
KT1	1.3804	1.3855	-0.37	0.25	0.32
KT2	1.8761	1.87179	0.23		
KT3	1.5884	1.5807	0.48		
KT4	1.66	1.6536	0.39		
KT5	1.8674	1.8622	0.28		
KT6	1.8606	1.8534	0.39		
KT7	1.0573	1.0505	0.64		
KT8	1.296	1.2969	-0.03		

Friability test is preformed in order to monitor the resistance of tablets to stresses like mechanical shocks and abrasion during the manufacturing, packing and transportation processes. Such stresses can lead to capping, chipping, abrasion or even breakage of the tablets. It is therefore important that the tablet is formulated to withstand such stress without damage. Among all the brands of Ketorolac Tromethamine, KT2 and KT5 showed less friability percentage. It means that they had higher durability than other brands. KT1 and KT8 had also less friability percentage. KT4 and KT6 had same friability percentage and that was 0.39. All the brands had shown their friability variation within ±1% range specified by USP (USP, 2007). Standard deviation was calculated among all the brands which were very close to individual percentage friability of all the brands.

CONCLUSION

All the tablets displayed uniformity in terms of hardness and weight variation and met USP standards for friability. Therefore it can be concluded that all the brands of the Ketorolac Tromethamine tested have uniform weight and also sufficient physical stability to maintain physical integrity over time and they will also be capable of withstanding the rigors of mechanical shocks encountered in its production, packaging, shipping and dispensing. Further studies should be conducted to test the potency and dissolution profile of the brands to confirm their pharmaceutical equivalence.

REFERENCES

Apurba SA, Nazmul HK, Monjurul K, Nani GB, Khandoker SM, A.T.M. Jamaluddin and Zakiur R. In Vitro Evaluation of the Pharmaceutical Equivalence of Phenoxymethylpenicillin Tablet Formulations Available in Bangladesh. JPR. 2011; 4(5):1445-1447.

American Society of Health-System Pharmacists. NSAID, retrieved from http://www.drugs.com/monograph/ketorolac-tromethamine.html, 2007; 05-11, 19-20.

Lachman L. Tablets, The theory and practice of Industrial Pharmacy. Varghese publication. (1986) 293-347.

Levi L, and Walker G. Quality controls of pharmaceuticals.The Canadian Medical Association, Le journal de L association medicale canadienne, 2010; 91(15).

Luthra V. Quality definition with objectives and manufacturing retrieved from http://www.businessdictionary.com/definition/quality.html. 2007; 01-02.

MHRA. Drug Safety Update. Retrieved from www.en.wikipedia.org, 2007; 1(3):03-04.

Marx K, Engels F, and Soch. The free dictionary by Farlex. 2nd ed. Retrieved from http://encyclopedia2.thefreedictionary.com/Quality, 2010; 23: 547.

Rooks WH, Maloney PJ, Shott LD, Schuler ME, Sevelius H, Strosberg AM, Tanenbaum L, Tomolonis AJ, Wallach MB, Waterbury D, et al. The analgesic and anti-inflammatory profile of ketorolac and its tromethamine salt. Drugs Exp Clin Res. 1985; 11(8):479-92

The American Society of Health-System Pharmacists. "Ketorolac-tromethamine". http://www.drugs.com/monograph/ketorolac-tromethamine.html. Retrieved 3 April 2011

US Pharmacopoeia. USP-NF-an overview, USP 33- NF 28th edition, Retrieved from http://www.usp.org/USPNF/, 2010; 01.

United State Pharmacopoeia 30 National Formulary 25. Rockville: United StatePharmacopoeial Convention Inc; 2007.

World Health Organization. Trade, foreign policy, diplomacy, health and quality of pharmaceutical products, retrieved from www.who.trade/glosary, 2010; 01-02.

Yoshida I and Sakai Y. The applications of the content uniformity test and the weight variation test on process validation tests of multiple ingredient preparations. Chem Pharm Bull. 1999; 47(5): 678-83.