



## **IN VITRO COMPARATIVE SYUDY OF QUALITY CONTROL PARAMETERS OF SOME BRAND OF KETOROLAC TABLETS AVAILABLE IN BANGLADESH**

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### **ABSTRACT**

Ketorolac is a non-steroidal agent with potent analgesic and moderate anti-inflammatory activity. It is administered as the tromethamine salt orally, intramuscularly, intravenously and as a topical ophthalmic solution. Six different sample brands marketed in Bangladesh were used to evaluate their comparative characteristics in different quality control parameters. The prime objective of the present study was to evaluate and compare the physicochemical parameters of different tablets of different brands that are available in local market of Bangladesh. General physicochemical parameters like thickness,

diameter, weight variation, hardness, friability, disintegration time, dissolution were evaluated to ensure quality tests of tablets. All the brands complied with the official specification for friability, uniformity of weight and disintegration time. The safety and efficacy of drug was determined by means of content assay. Potency was determined by using UV method. The potency of ketorolac in six brands was within acceptable range ( $102.32 \pm 0.35\%$ ,  $95.76 \pm 0.21\%$ ,  $100.56 \pm 0.58\%$ ,  $98.73 \pm 0.46\%$ ,  $104.29 \pm 0.90$ ,  $97.76 \pm 0.13\%$ ). All the brands showed better dissolution profile as they released more than 75% drug in 45 min. The study revealed that most of the marketed ketorolac tablets met the standards for physical properties which are the indicators of drug quality.

**KEYWORDS:** ketorolac, physicochemical parameters, potency, dissolution profile.

### **INTRODUCTION**

Quality control is a process that is carried out to ensure a desired level of quality in a product or service. It might include whatever actions a business deems necessary to provide for the

control and verification of certain characteristics of a product or service.<sup>[1]</sup> Most often, it involves thoroughly examining and testing the quality of products or the results of services. ISO 8402-1986 standard defines that quality is the totality of features and characteristics of a product or service that bears its ability to satisfy stated or implicated needs.<sup>[2]</sup>

A tablet is a pharmaceutical dosage form. It comprises a mixture of active substances and excipients, usually in powder form, pressed or compacted into a solid. Tablets Dosage form is one of a most preferred dosage form all over the world. Almost all drug molecules can be formulated in a tablet and process of manufacturing of tablets is very simple, and is very flexible. One can administered 0.01 mg of a drug dose to 1 gm of a drug dose by oral route of administration, by formulating as a tablet.<sup>[3]</sup>

Ketorolac tromethamine is a member of the pyrrolo-pyrrole group of NSAID (Nonsteroidal Anti-inflammatory Drug).<sup>[4]</sup> Ketorolac Tromethamine is chemically, 5-Benzoyl-2, 3 - Dihydro- 1 H -Pyrolizine- 1- Carboxylic Acid, 2Amino-2-(hydroxymethyl)-1, 3- Propanediol.<sup>[5]</sup> Ketorolac tromethamine is a non-steroidal anti-inflammatory drug that belongs to the class of heteroaryl acetic acid derivatives. It is a non-selective cyclooxygenase (COX) inhibitor, being marketed in the racemate form. Most of its analgesic and COX inhibitory activity is retained in the S-isomer. Ketorolac is administered as its tromethamine salt orally, intramuscularly, intravenously and as a topical ophthalmic solution. The frequent occurrence of gastrointestinal disturbances including gastrointestinal bleeding, perforation and peptic ulceration along with the short mean plasma half-life ( $t(1/2)$  approximately 5.5 h) has prompted for the development of various formulation strategies for the appropriate delivery of Ketorolac.<sup>[6]</sup> Ketorolac is frequently used as analgesic drug in pregnancy and postpartum period.<sup>[7]</sup>

The onset of ketorolac analgesia is much slower than the onset of opioid analgesia. Compared with opioids, ketorolac 30 mg exhibited analgesic activity and pain relief equivalent to that of meperidine.<sup>[8]</sup> 50 mg and 100 mg intramuscularly and may be more cost-effective than intravenous morphine. Ketorolac tromethamine has a pKa of 3.5 and an n-octanol/water partition coefficient of 0.26. A single 10 mg tablet given orally to human volunteers following surgery provided pain relief equivalent to that provided by 10 mg of morphine given intramuscularly. When given intramuscularly to rabbits (0.25 ml of a 0.31-5% solution) or man (3 ml of a 1-3% solution), no drug-related irritation or changes in creatine phosphokinase were seen. Solutions (less than or equal to 0.5%) applied to the eyes of

animals and man were not irritating. When applied topically in rat and rabbit models of ocular inflammation, less than or equal to 0.5% solutions of ketorolac tromethamine inhibited the inflammatory response.

The intention of the study is to make a assimilation of product quality control parameters, specify visual uniqueness and substantiate differences in physicochemical properties between different marketed ketorolac tromethamine tablets in Bangladesh.

## **MATERIALS AND METHOD**

### **Recruitment of sample product**

The marketed sample of six brands of Ketorolac tablet were purchased from local medicine shop at Dhaka in Bangladesh. These tablets of six brands were coded as M1, M2, M3, M4, M5, and M6. The samples were properly checked for their physical appearance, name of manufacturer, batch number, and manufacturing date, expiry date, manufacturing license number, D.A.R. number & maximum retail price. There are approximately forty different brands of ketorolac tromethamine available in pharma market of Bangladesh (according to BD.DRUGS.COM). Here six different available brands are chosen from well known pharmaceutical company of Bangladesh.

### **Weight variation test**

For each brand, 10 tablets were randomly and weighted individually using an analytical balance (TE214S, sartorius Germany). The average weights were determined using the following formula.

$$X = (X_1 + X_2 + X_3 + \dots + X_n) / 10$$

Then the percentage weight deviations were determined by using the following formulas.

% of Deviation (+) = (maximum weight- average weight)/average weight  $\times$  100.

% of Deviation (-) = (minimum weight- average weight)/average weight  $\times$  100.

### **Hardness test**

10 tablets were taken randomly and hardness was measured using automatic Hardness Tester (VEEGO, INDIA). The hardness of tablets, which is the force required to break a tablet in a diametric compression force. If the tablet is too hard, it may not disintegrate in the required period of time or meet the dissolution specification; if it is too soft, it will not withstand the

handling during subsequent processing such as coating or packaging and shipping operations.<sup>[9]</sup>

### **Friability test**

Friability test should be performed to evaluate the ability of Ketorolac tablet to withstand abrasion during packaging, handling & transporting. 20 Ketorolac tablets were taken randomly & weighted together. Ketorolac tablets were then placed into the Roche friabilator & subjected to 100 rpm for 1 minute at Ketorolac tablets were reweighted. This loss of weight indicates the friability of Ketorolac tablet. Finally the percent of weight of loss was calculated by following way.

$$\% \text{ of Weight loss} = \frac{(\text{Initial weight} - \text{Final weight}) \times 100}{\text{Final weight}}$$

### **Disintegration Test**

Disintegration test is performed to find out that within how much time the Ketorolac tablet disintegrates. Disintegration test is very important for all coated & uncoated tablet because the dissolution rate of drug depends on the disintegration time, which ultimately affect the rate of absorption of drug. About 600ml distilled water was taken in both 1000ml beaker & then these beakers were placed into the device. One Ketorolac tablet was placed in each tube of basket rack & a plastic disk was placed over each tablet & then the basket rack was accurately positioned into the beaker. The temperature was maintained as 37 °C i.e. body temperature. The time at which all the Ketorolac tablets passed through the sieve was the disintegration time & the average disintegration time were calculated.<sup>[9]</sup>

### **Potency test**

Ten tablets of each brand were taken and the average weight was determined. Those ten tablets of each brand were crushed in mortar and pestle. Amount of powdered tablet containing equivalent to 10 mg of Ketorolac drug was determined by calculation. Determined amount of powdered tablet was taken in 100 ml volumetric flask and distilled water was added up to 100 ml. Solution was filtered and 20 ml filtrate was taken in a test tube and was diluted with 100 ml of distilled water. Absorbance of the sample was determined at 276 nm wavelength.<sup>[9]</sup>

### **CALCULATION**

**% of potency = Conc. (mg/ml) x dilution factor x total volume x average weight x 100/(sample taken x strength)**

**Dissolution test**

About 600ml of distilled water was filled into 1000ml beaker(because water is used as media) of dissolution apparatus. (USP, 2013) One Ketorolac tablet was placed into each beaker. 37 °C i.e. body temperature & 50rpm i.e. rotation per minute was adjusted & then motor was started. 10ml solution was withdrawn from beaker and replaced with 10ml distilled water & then withdrawn solution was immediately filtered. The withdrawn solution of Ketorolac tablet was 10 times diluted & absorbance was measured at 276nm by using UV spectrophotometer. Finally the percent release of Ketorolac tablet was determined by following equation.

$$\% \text{ of release} = \text{drug cont. (mg)} \times 100 / \text{strength (mg)}$$

**RESULT AND DISCUSSION****Weight variation determination**

Tablet weight is mainly affected by factors such as tooling of the compression machine, head pressure, machine speed and flow properties of the powder. Inconsistent powder or granulate density and particle size distribution are common sources of weight variation during compression. Variation between tablet with respect to dose and weight must be reduced to a minimum. Uniformity of weight is an in process test parameter which ensures consistency of dosage units during compression. The average weight of tablets of each brand was between 130mg-324 mg and usp specification for weight variation of tablets  $\pm 7.5\%$  for the average weight range. All brands comply with the specification according to USP.

**Hardness test**

Hardness was monitored using a Automatic Tablet hardness Tester (Dr. Schleunigerd, Switzerland).(Table 2)

**Friability test**

It is the tendency for a tablet to chip, crumble or break following compression. This tendency is normally confined to uncoated tablets and surfaces during handling or subsequent storage. The USP specification for friability test is 1%. It was monitored that six different brand of ketorolac tablets were in accordance with USP guideline. (Table 2)

**Disintegration test**

Disintegration tests are performed as per the pharmacopoeial standards. Disintegration is a measure of the quality of the oral dosage form like tablets and capsules. Each of the

pharmacopoeia like the USP, BP, IP etc. each have their own set of standards and specify disintegration tests of their own. The disintegration test is performed to find out the time it takes for a solid oral dosage form like a tablet or capsule to completely disintegrate. The time of disintegration is a measure of the quality. This is because, for example, if the disintegration time is too high; it means that the tablet is too highly compressed or the capsule shell gelatin is not of pharmacopoeial quality or it may imply several other reasons. And also if the disintegration time is not uniform in a set of samples being analyzed, it indicates batch inconsistency and lack of batch uniformity. According to USP, 2013 the specification of disintegration time requirements 5 to 30 minutes. All the tablets that have been tested are within the limit. (Table 2)

### Potency test

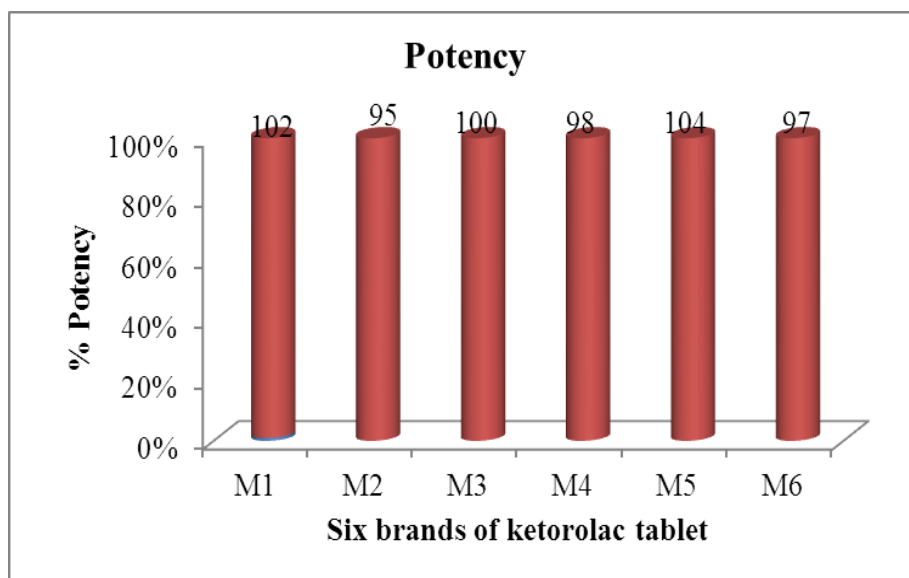
Potency of all brands was found within 95.34–103.65%. USP specification for the drugs are equivalent to not less than 95.0 percent & not more than 105.0 percent. Six brands are within the limit of potency according to the USP specification. (Table 1)

### Dissolution test

Dissolution is a test used by the Pharmaceutical industry to characterize the dissolution properties of the active drug, the active drug's release and the dissolution from a dosage formulation. Dissolution testing is used to formulate the drug dosage form and to develop quality control specifications for its manufacturing process. The USP specification of ketorolac tromethamine is not less than 75% of the labeled amount of is dissolved in 45 minutes. It is seen from the result that all brand of Ketorolac tablets meet the specification. (Table 3)

**Table 1: potency and weight variation of different brands of ketorolac tablet collected from local market in Bangladesh.**

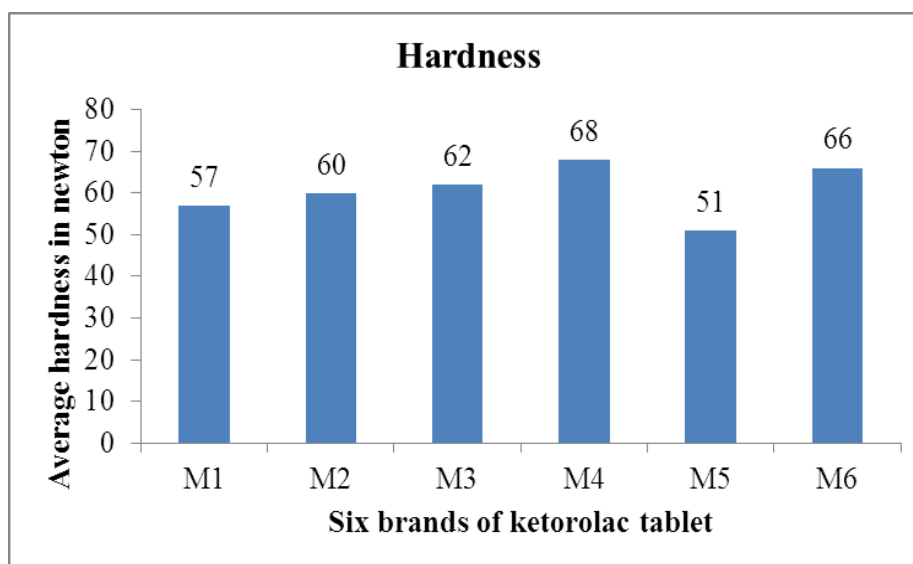
Tablets	Potency	Weight variation
M1	102.32±0.35	185.45±0.76
M2	95.76±0.21	165.2±0.45
M3	100.56±0.58	130.9±0.36
M4	98.73±0.46	173.9±0.21
M5	104.29±0.90	243.25±0.76
M6	97.76±0.13	166.00±0.44



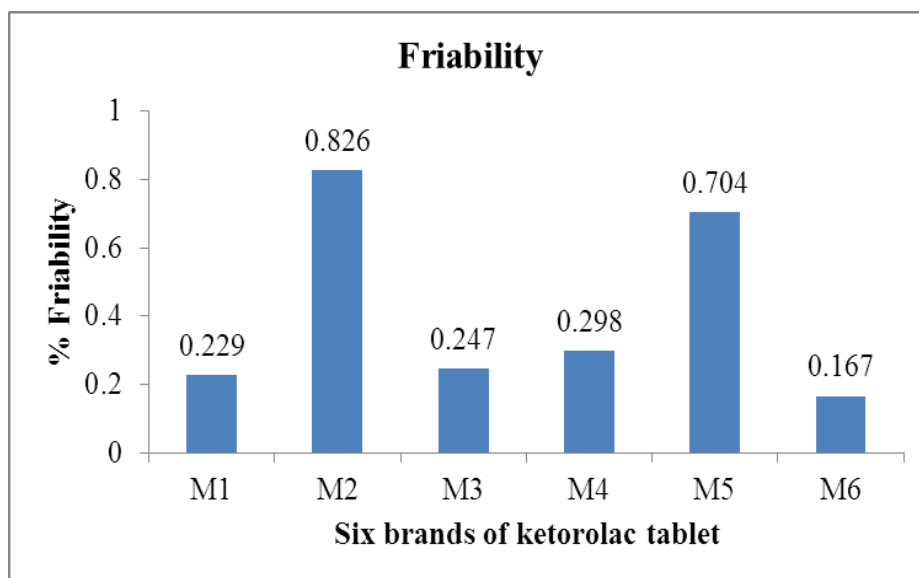
**Fig 1: Determination of potency of six brands of ketorolac tablet.**

**Table 2: hardness, friability and disintegration of ketorolac tromethamine tablet:**

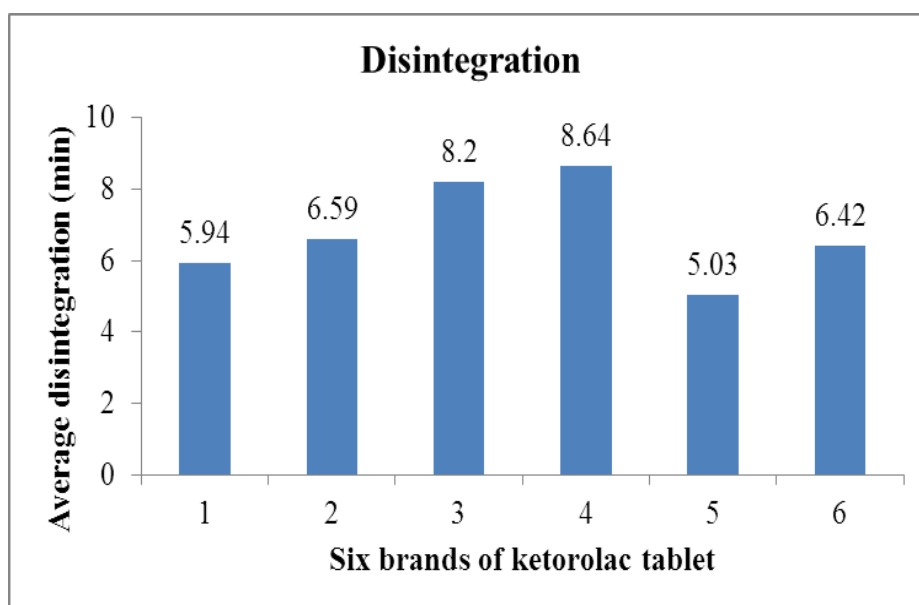
Tablets	Hardness(N)	Friability(%)	Disintegration(min)
<b>M1</b>	57.95±0.23	0.229	5.94±0.81
<b>M2</b>	60.38±0.12	0.826	6.59±0.55
<b>M3</b>	62.21±0.31	0.247	8.20±0.65
<b>M4</b>	68.33±0.57	0.298	8.64±0.75
<b>M5</b>	51.33±0.36	0.704	5.03±0.83
<b>M6</b>	66.33±0.18	0.167	6.42±0.55



**Fig 2: Average hardness of six brands of Ketorolac tablet.**



**Fig 3: Friability of six brands of ketorolac tablet.**



**Fig 4: Average disintegration time of six brands of ketorolac tablet.**

**Table 3: Average drug release (%) of six different brands of ketorolac tablets**

Time (min)	% Drug Release					
	M1	M2	M3	M4	M5	M6
0	0	0	0	0	0	0
5	34.26±0.22	27.57±0.66	24.8±0.43	42.69±0.57	30.50±0.86	27.34±0.76
15	48.09±0.25	43.43±0.63	51.39±0.45	56.50±0.58	62.54±0.87	41.02±0.72
30	70.03±0.23	57.6±0.60	73.6±0.48	71.54±0.58	78.31±0.88	62.89±0.73
45	89.05±0.24	86.5±0.67	84.41±0.44	87.31±0.55	89.02±0.89	90.25±.77
60	101.48±0.27	100.97±0.69	98.02±0.45	100.02±0.53	101.50±0.88	100.70±0.73



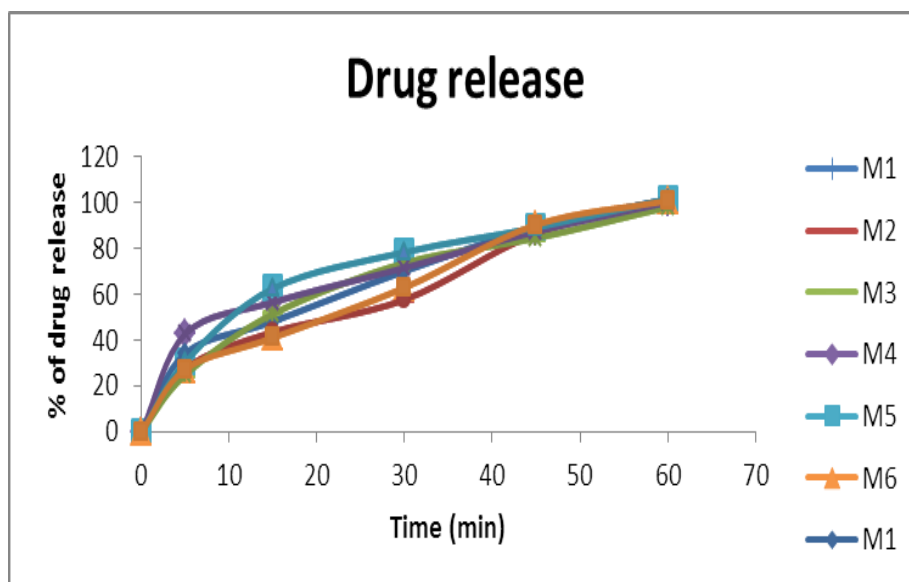


Fig 5: Drug release (%) of six brands of ketorolac.

## CONCLUSION

All the tablets asserted uniformity in terms of hardness, potency, dissolution, disintegration, friability and weight variation and met USP standards. 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 stiffness of mechanical shocks confrontation in its production, packaging, shipping and dispensing.

## REFERENCE

1. Hasan A, Dewan SAR, Ahamed SK, Kai MM. Quality control studies on cetirizine hydrochloride tablets available in Bangladesh drug market. *International Journal of Pharmacy and Biological Sciences*, 2013; 3(1): 349-354.
2. Nasrin N, Asaduzzaman M, Mowla R, Rizwan F, and Alam A. A comparative study of physical parameters of selected ketorolac tromethamine tablets available in the pharma market of Bangladesh. *Journal of applied pharmaceutical Sciences*, 2011; 01(08): 101-103.
3. Kamble N, Chaudhari PS, Oswal RJ. Innovations in Tablet Coating Technology. *International Journal of Pharmaceutics*, 2000; 2(1): 114-117.
4. Data base of Drug Bank of Ketorolac. <https://www.drugbank.ca/drugs/DB00465>.
5. Narasimharao R, Somashekar S, Prakash K. Design and evaluation of Keterolac Tromethamine impregnated Hydroxy Propyl Methyl Cellulose films. *Journal of Chemical and Pharmaceutical Research*, 2011; 3(1): 360- 381.

6. Sinha VR, Kumar RV, Singh G. Ketorolac tromethamine formulations: an overview. *Expert Opinion on Drug Delivery*, 2009; 6(9): 961–75.
7. Soldin OP, Mattison DR. Sex differences in pharmacokinetics and pharmacodynamics. *Clinical Pharmacokinetic*, 2009; 48(3): 143–57.
8. Rainer TH, Jacobs P, Ng YC, Cheung NK, Tam M, Lam PK. Cost effectiveness analysis of intravenous ketorolac and morphine for treating pain after limb injury: double blind randomized controlled trial. *BMJ*, 2000; 321(7271): 1247–51.
9. The United States Pharmacopeia (USP). The United States Pharmacopeial Convention: 12601 Twinbrook Parkway, Rockville, 2013; 3731-3733.