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RELEASE PATTERN AND POTENCY STATUS OF SOME DICLOFENAC SODIUM ENTERIC COATED TABLETS OF THE PHARMA-MARKET OF BANGLADESH

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Abstract: Fifteen brands of commercially available Diclofenac Sodium enteric-coated tablets were purchased from different regions of Bangladesh and were studied for their in-vitro release behaviors as well as for their potency status. Of the fifteen samples, three (DS-03, DS-10, DS-15) were found noncompliance in respect of disintegration test requirements of USP (United States Pharmacopoeia). All of the brands complied with the USP dissolution specifications for their drug release in the simulated gastric fluids and intestinal fluids except four brands (DS-03, DS-05, DS-10, DS-15) and were found to be substandard in respect of dissolution test. DS-05 complied with the compendial specification in respect of drug release in gastric fluid but failed to comply in intestinal fluids (76.97%). According to BP (British Pharmacopoeia), two brands (DS-10, DS-15) were found to be substandard in respect of potency.

Key Words: Diclofenac Sodium; enteric-coated tablets; disintegration test; dissolution test; potency estimation.

Introduction

There has been a tremendous demand of enteric-coated products in the pharmaceutical market (Ridwan Ullah, 2001). The rational of enteric coating of the drug is to resist dissolution and disintegration in the stomach but not in the intestines, thereby allowing for tablet transit through the stomach intact. Enteric-coated tablets should be intact in gastric fluid; which can be revealed by disintegration and dissolution tests (Chambliss *et al*., 1984). It is also possible to correlate disintegration and dissolution rates with biological activity of the active ingredient (Ayres *et al*., 1984).

Reports on the existence of substandard drugs are very common in national dailies and weeklies of•Bangladesh (The Daily Ittefaq, 1999; The Daily Sangbad, 1993). The reports on ampicillin (Roy *et al*., 1994), amoxicillin (Hossain *et al*., 1999) metronidazole and sulfadiazine (Safiullah *et al*., 1987), hyoscine and aspirin (Safiullah *et al*., 1986), antacid (Malik *et al*., 1987), metoclopramide (Nargis *et al*., 1997) and paracetamol (Pijus Saha *et al*., 2002) revealed the existence of substandard drugs. Dissolution analysis of pharmaceutical dosage forms has now emerged as a very important test for product quality (Ayes & Hsu, 1989). A large number of reports on the drug release profile on marketed products in terms of dissolution and disintegration have been published (Gouda *et al*., 1980; Juhl *et al*., 1980; Romero *et al*., 1998; Wood *et al*., 1990).

Diclofenac Sodium (DS), a phenyl acetic acid derivative non-steroidal drug of choice having marked anti-inflammatory, analgesic and antipyretic activity that are widely prescribed now a days (Liu *et al*., 1995; Miyagwa *et al*., 1996). Thus a study was undertaken to evaluate the quality of marketed Diclofenac Sodium enteric-coated tablets in terms of disintegration time, dissolution profile and drug content.

Materials and Methods

Sample: Fifteen brands of Diclofenac Sodium enteric-coated tablets were purchased from the markets of different regions of Bangladesh. The areas including Paikgacha (Khulna), Daulatpur (Khulna), Fultala (Khulna), Heraj Market (Khulna), Keshabpur (Jessore), Tala (Sathkhira), Savar and Mitford (Dhaka). The samples were collected from June, 2001 to March, 2003 in such a way that some samples were immediately after manufacturing, some were just before their expiry dates and others were intermediate of two kinds to know also about the stability status of the drug products during their shelf-life. The labels of all the products claimed to contain 50 mg of Diclofenac Sodium per tablet.

Chemicals: Diclofenac Sodium used as a reference standard for the construction of standard curves was obtained from Desh Pharmaceuticals (Pvt.) Ltd., Dhaka, Bangladesh. Disodium hydrogen phosphate, potassium dihydrogen phosphate and trisodium phosphate dihydrate have been purchased from E. MERK (India) Ltd. A pH 1.2 solution (2.0 g NaCl and 7 ml conc. HCl per 1000 ml) was used as the simulated gastric fluid and a pH 7.5 buffer (8.05 g Na_2HPO_4 and 1.65 g $NaH_2PO_4.2H_2O$ per 1000 ml) was used as the simulated intestinal fluid (Nargis *et al*., 1993).

Disintegration Studies: Disintegration test was carried out by Thermonic Tablet Disintegration Test Unit, Campbell Electronics, Mumbai, India (USP 23, 1995).

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Dissolution studies: *In-vitro* drug release studies were conducted using type II dissolution apparatus at 37±0.5°C at 50 rpm (USP 23, 1995). Sampling was done in a predetermined rate and absorbance was measured using a UV spectrophotometer at 277 nm. The dissolution studies were carried out in simulated gastric and intestinal fluids (Nargis *et al.*, 1993). The amount of the drug dissolved was calculated with the aid of calibration curves constructed from standard solutions of different concentration of the drug in the respective dissolution media.

Potency studies: A UV spectrophotometer (Camspec, UK) was used to determine the amount of Diclofenac Sodium present in the samples at 277 nm and compared with the standard Diclofenac Sodium sample (BP, 2000). The experiments were conducted in the Bio-pharmaceutics Laboratory of the Pharmacy Discipline, Khulna University, Khulna-9208, Bangladesh.

Results and Discussion

The results of disintegration test of the fifteen samples of Diclofenac Sodium tablets were shown in Table 1. And it was observed that 3 brands (20% of the samples) did not comply with USP specification. The poor disintegration properties of the commercial brands (DS-03, DS-10, DS-15) may be due to improper selection of the disintegrating agents. Those brands, which passed the acid stage tests also passed the buffer stage tests.

On the other hand, two brands (DS-05 and DS-13), 13.33% had shown prolonged disintegration time at the buffer stages.

Table 1. Result of Disintegration Test of the Samples of Diclofenac Sodium Enteric-coated Tablets.

Sample code	No.•of tested tablets	Acid stage	Buffer stage	Observation
		Condition after 2 hours	DT±SD (min)	
DS-01	6	Intact, only color was diminished.	4.30±0.80	Compliance
DS-02	6	Intact, color was intact.	7.10±1.49	Compliance
DS-03	6	Crack found and disintegrated	----------	Noncompliance
DS-04	6	Color was disrupted but coating was intact	9.17±3.67	Compliance
DS-05	6	Intact, no cracking	54.00±1.82	Compliance
DS-06	6	Intact, no cracking	33.83±1.77	Compliance
DS-07	6	Color was disrupted but coating was intact	37.50±2.06	Compliance
DS-08	6	Intact, no cracking.	21.30±3.18	Compliance
DS-09	6	Intact, no change	5.80±1.43	Compliance
DS-10	6	Disintegrated	----------	Noncompliance
DS-11	6	Color was disrupted but coating was intact	12.00±1.63	Compliance
DS-12	6	Intact	2.25±0.48	Compliance
DS-13	6	Color was disrupted but coating was intact	46.17±3.58	Compliance
DS-14	6	Intact	19.58±1.54	Compliance
DS-15		Tablets disintegrated	----------	Noncompliance

DT = Disintegration Time, SD = Standard Deviation

Three (20%) of the tested samples (DS-03, DS-10, DS-15) did not comply with USP specification. At acid stage 45.85 %, 49.84 % and 58.67 % of Diclofenac Sodium were released from DS-03, DS-10, DS-15 respectively. The remaining samples complied dissolution specification at acid (gastric fluids) and buffer (intestinal fluids) stages except DS-05, which released 76.97 % of drug after 60 minutes at the buffer stage. Dissolution is the prime factor for proper absorption of the drug particles by the intestine and ultimately bio-availability of the drugs (Miyagawa *et al.*, 1996) and such a poor dissolution properties of the commercial brand (DS-05) may be due to improper selection of formulation ingredients as well as incorrect manufacturing procedure. Based on the disintegration and dissolution results, it may be pointed out that 4 brands, DS-03, DS-05, DS-10, DS-15, (26.67%) showed noncompliance with the USP specification.

The amount of Diclofenac Sodium present in the sampled tablets was shown in Table 2. Two samples (DS-10, DS-15) did not comply with the BP specification in respect of potency. The low potency may be due to the addition of inadequate quantity of the Diclofenac Sodium initially or may be due to the degradation of the drug during their shelf-life period.

The dissolution pattern of the fifteen samples was illustrated in Fig.1 to Fig. 3.

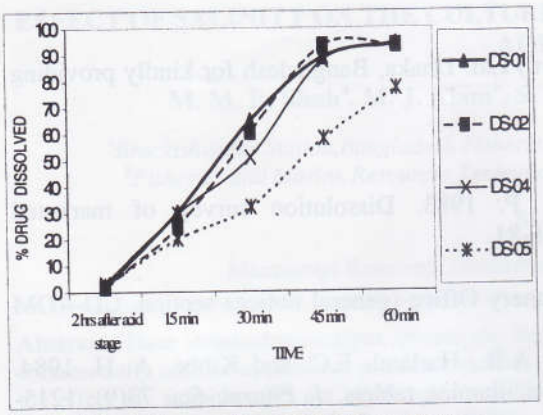

Fig.-1. Dissolution profile of Diclofenac Sodium tablets (DS-01 to DS-05).

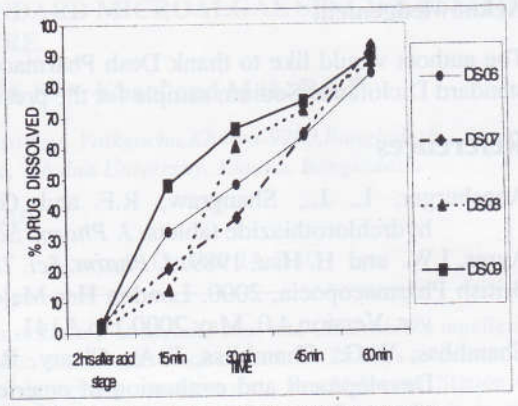

Fig.-2 Dissolution profile of Diclofenac Sodium tablets (DS-06 to DS-10).

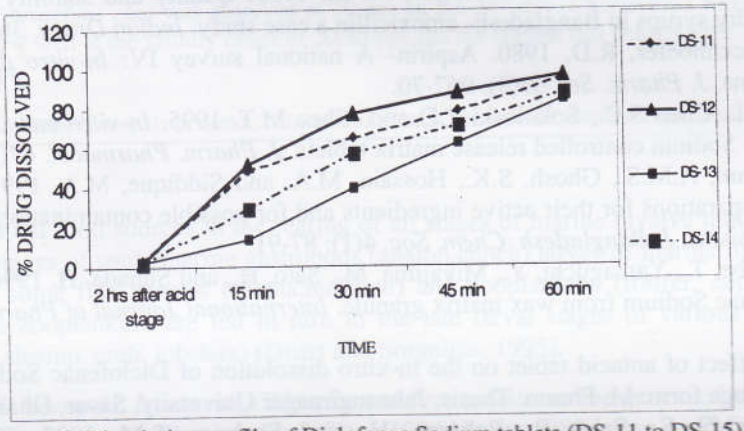

Fig.- 3. Dissolution profile of Diclofenac Sodium tablets (DS-11 to DS-15).

Table 2. Potency Status of the Samples of Diclofenac Sodium Enteric- coated Tablets

Sample code	Declared amount per tablet (in mg)	Estimated amount of Diclofenac Sodium per tablet (in mg)	Percent Deviation	Observation
DS-01	50	50.46	+0.91	Compliance
DS-02	50	47.71	-4.41	Compliance
DS-03	50	49.08	-1.85	Compliance
DS-04	50	48.61	-2.88	Compliance
DS-05	50	50.92	+1.83	Compliance
DS-06	50	51.68	+3.36	Compliance
DS-07	50	50.92	+1.83	Compliance
DS-08	50	49.23	-1.55	Compliance
DS-09	50	50.62	+1.21	Compliance
DS-10	50	47.08	-5.84	Noncompliance
DS-11	50	49.99	-0.02	Compliance
DS-12	50	49.08	-2.85	Compliance
DS-13	50	47.99	-4.01	Compliance
DS-14	50	48.92	-2.16	Compliance
DS-15	50	46.46	-7.07	Noncompliance

CONCLUSION

The present study did not cover all the commercially available Diclofenac Sodium enteric coated tablets of the Pharma-market of Bangladesh. Besides *in-vivo* bioavailability studies are of utmost importance to draw conclusion regarding quality status of the samples. Although the study was done on a limited scale, on the basis of professional judgment, it may be opined that constant surveillance on marketed Diclofenac Sodium and the marketed drugs by the Govt., Manufacturers, Pharmacists, independent research groups or health professionals are necessary to ensure availability of quality drugs in the country.

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